NEW

PANDEMICS

THE HISTORY & SCIENCE BEHIND THE WORLD'S DEADLIEST OUTBREAKS

INSIDE
HOW THE COVID-19 VACCINE WORKS

CAN WE WIN THE WAR AGAINST VIRUSES?

BLACK DEATH
THE MEDIEVAL OUTBREAK THAT RAVAGED EUROPE

EXPOSED
FIND OUT HOW A VIRUS REALLY WORKS

COVID-19
INVESTIGATING ITS LEGACY

Digital Edition
FUTURE
SECOND EDITION

WARNING! PATHOGENS DETECTED

Proceed with caution. You are entering a zone where a number of dangerous pathogens will be handled, ranging from the Black Death and the Spanish flu to the latest menace to humanity, COVID-19. Please ensure that the necessary safety measures have been taken before studying the evolution of viruses, learning how the plague that struck medieval Europe was cured and uncovering which diseases are now being targeted by the WHO. It is advised that you prepare yourself before examining precisely what viruses are and how the immune system and vaccines work to fight them off. Special precautions may be required before the final stage of your journey, in which you will explore whether viruses are currently flourishing in space and discover why some viruses are in fact necessary for the existence of life.


FUTURE

PANDEMICS

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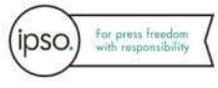
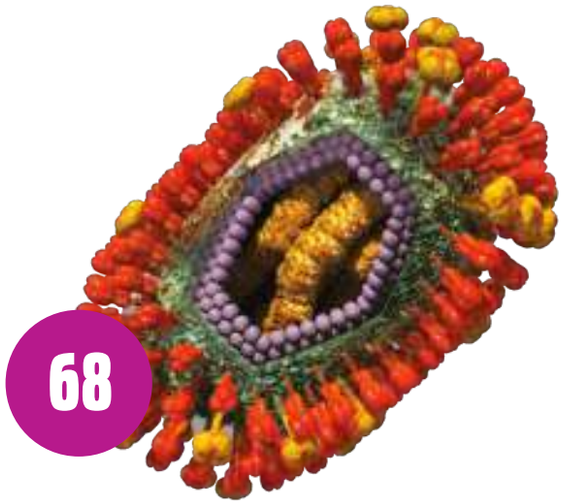


All content previously appeared in this edition of **Virus**

CONTENTS

ANCIENT OUTBREAKS

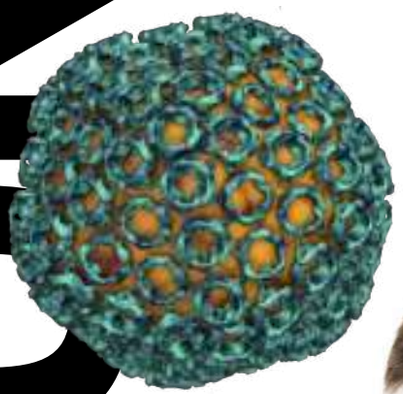


68

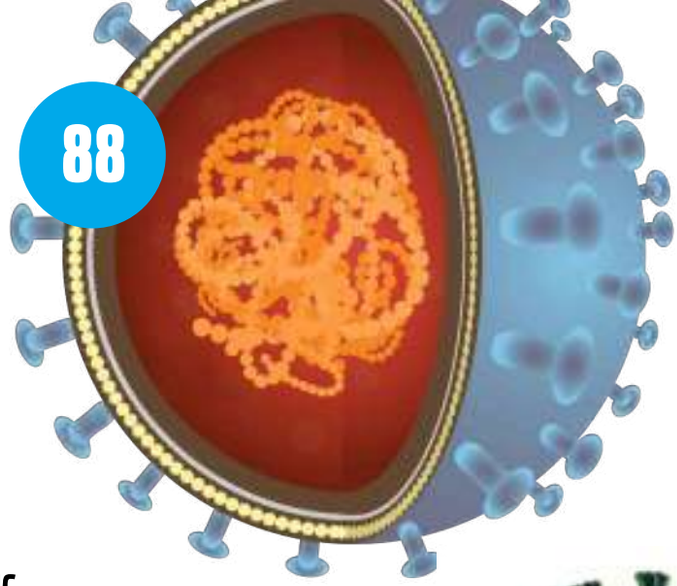
50

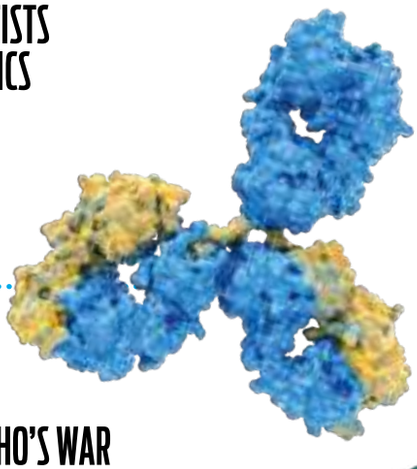
THE BLACK DEATH

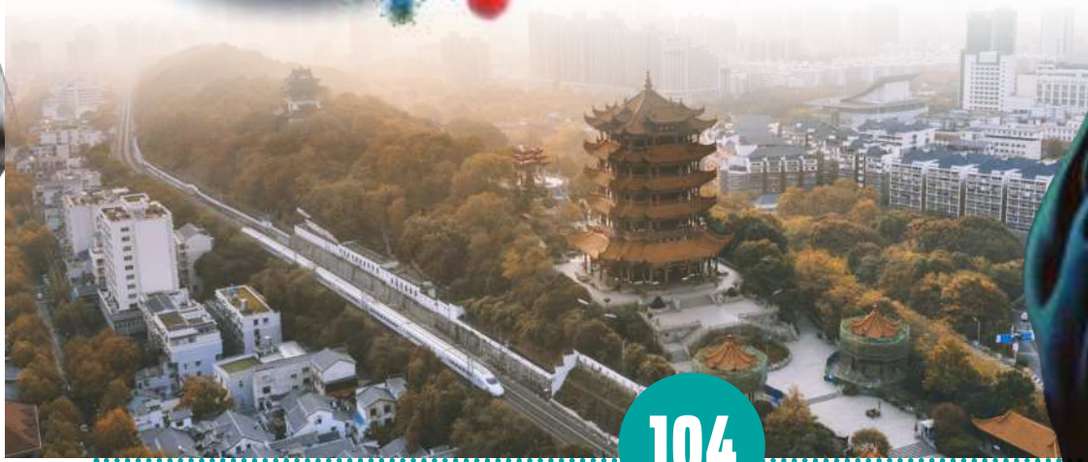
INFLUENZA



54





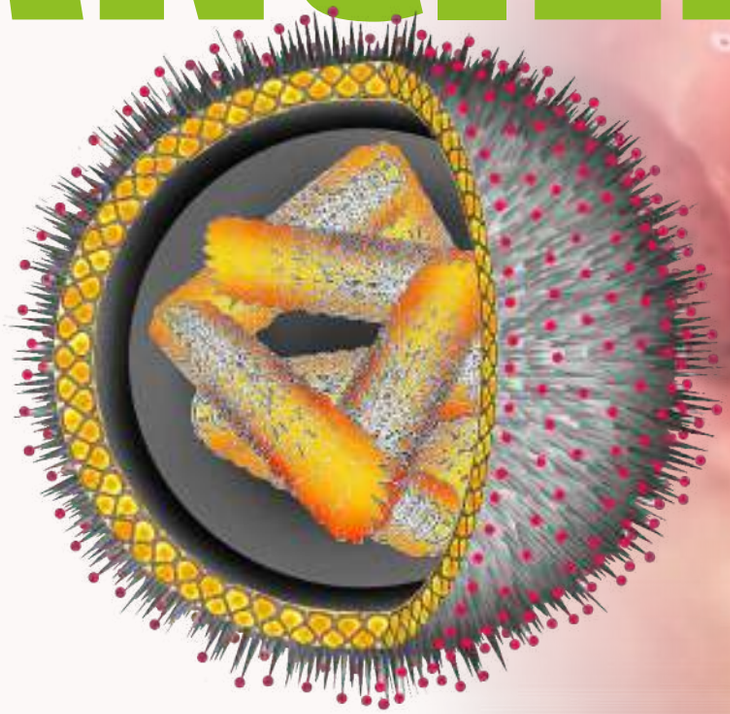


10

THE EVOLUTION OF VIRUSES

Find out when and how the very first viruses emerged on planet Earth

ANCIENT



OUTBREAKS

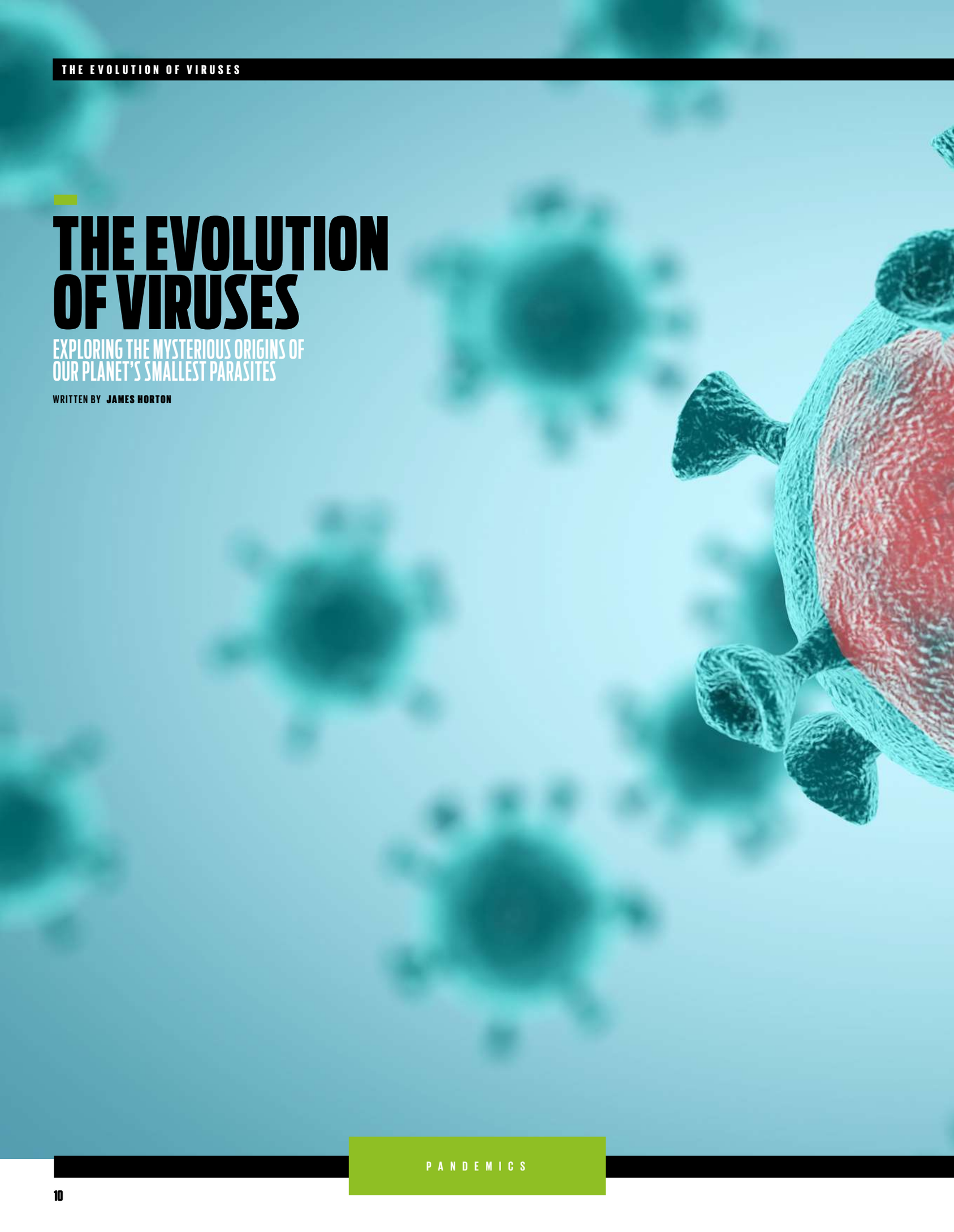
16
HISTORIC PANDEMICS

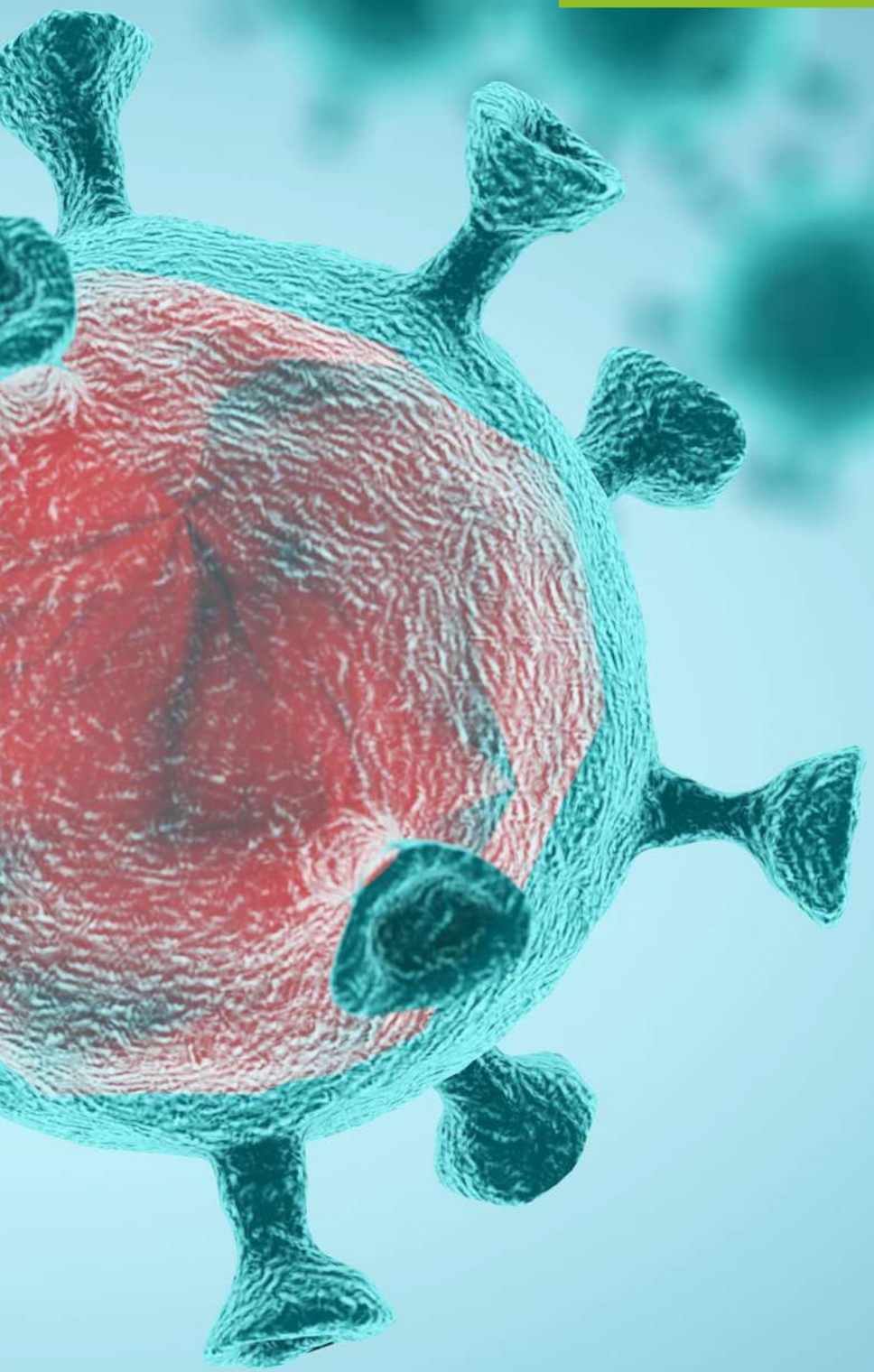
These devastating outbreaks claimed millions of lives across the world

THE EVOLUTION OF VIRUSES

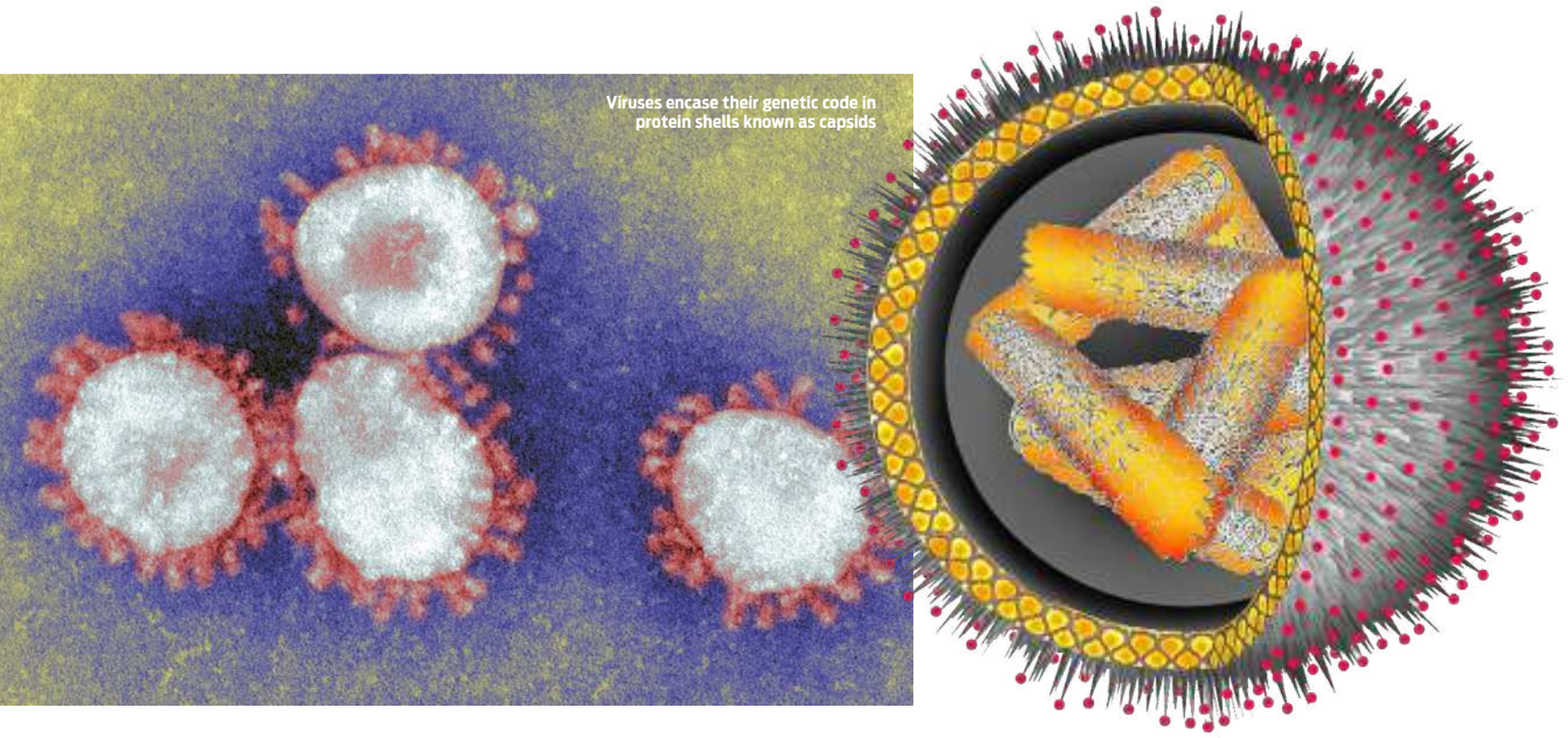
EXPLORING THE MYSTERIOUS ORIGINS OF OUR PLANET'S SMALLEST PARASITES

WRITTEN BY **JAMES HORTON**





There are multiple competing hypotheses that explain the origin of viruses



Viruses encase their genetic code in protein shells known as capsids

Viruses are curious biological entities. They are obligate parasites; unable to replicate on their own, they instead exist by hijacking the cellular apparatus of other cells to replicate and proliferate. As such, they are simplistic – so simple, in fact, that they don't satisfy all the criteria to be considered 'alive'. Viruses cannot synthesise adenosine triphosphate, a critical molecule used for carrying energy. They likewise do not possess the molecular equipment to perform translation, the process that uses information from the genetic code called ribonucleic acid (RNA) to synthesise proteins. Proteins are the workhorses of cellular life, and without them a cell is devoid of almost all activity. This absence is analogous to possessing a recipe book but having no kitchen appliances with which to cook. Lacking energy-carrying molecules and the ability to make proteins would be devastating to a self-sustaining organism, but viruses do not carry out any metabolic processes. Instead, when it's independent, a virus is just a small, lifeless husk of genetic material wrapped inside a meagre protein shell. If it were somehow to remain in isolation, it would soon dwindle to extinction.

Once a virus finds a host, however, it assumes a much more impactful role. They may not possess much complexity, but what viruses do have is the ability to infect cells and once inside take advantage of the cell's protein-building ability to replicate themselves. Unfortunately for the host cells, they are often the architects of their own destruction as their apparatus busily gets to work copying the virus' genetic material at the expense of itself. Some viruses are also able to integrate their own genetic material into their host cell's DNA, becoming an intrinsic part of it. These attributes make viruses the master manipulators of cellular life. This has allowed them to persist for many billions of generations despite being entirely dependent on other organisms for replication. Some viruses are so devastatingly effective at proliferating through this method that they're even capable of eradicating immensely complex multicellular life.

How did viruses evolve to be this way? Were they once fully equipped microorganisms that shed their molecular 'dead weight' and became parasites, or did they begin as just genetic code and gain a few fancy tools that helped them ensure their own replication? Or did viruses first evolve before even single-celled organisms, and those that persist today are mere relics of an ancient emergence of life?

THE PRECURSOR HYPOTHESIS

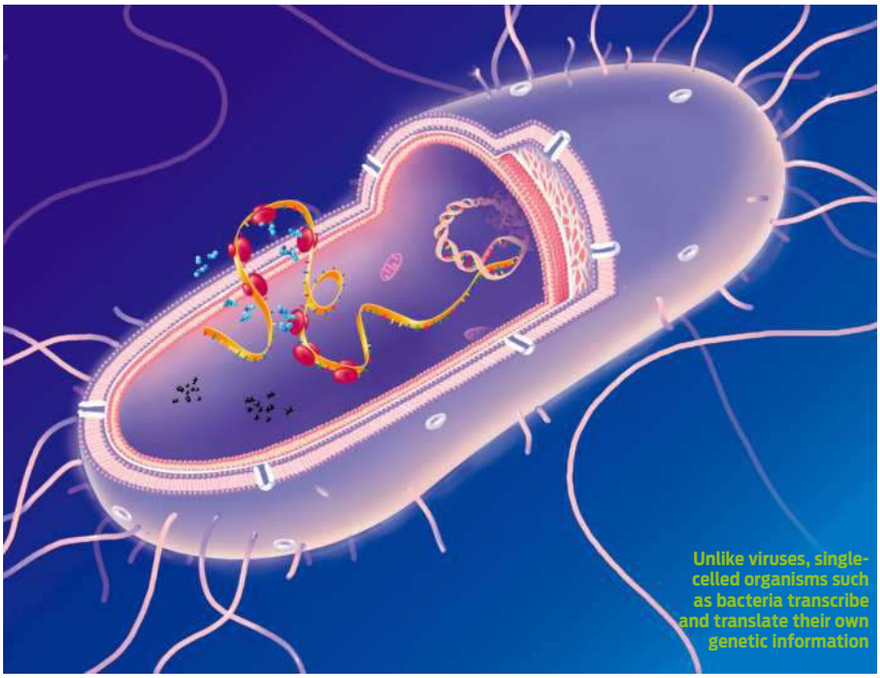
Genetic code is the basis of life on Earth. It is, as far as we understand, the first organic molecule capable of carrying swathes of chemical instructions and so underpins all life. Genetic code is made up of nucleic acids, DNA and RNA. In complex life, DNA is first transcribed into RNA, which then relays the chemical instructions to molecules called ribosomes that form proteins. In this setup, RNA is the intermediate component, but it's now believed that RNA was the first nucleic acid to exist at the origin of life. Scientists have also identified a group of RNA molecules known as ribozymes that can catalyse chemical reactions – a job principally performed by proteins. Therefore, at the origin of life, the very first entities may not have needed DNA or proteins at all in order to replicate.

If such self-replicating units existed prior to the evolution of the very first cells, they may have been primed to infect these cells once they appeared. Therefore, the parasitic role of the virus may have been established as soon as they first contacted cellular life. Some viruses still solely use RNA as their genetic code and may be the closest descendants to their ancient parasitic forerunners.

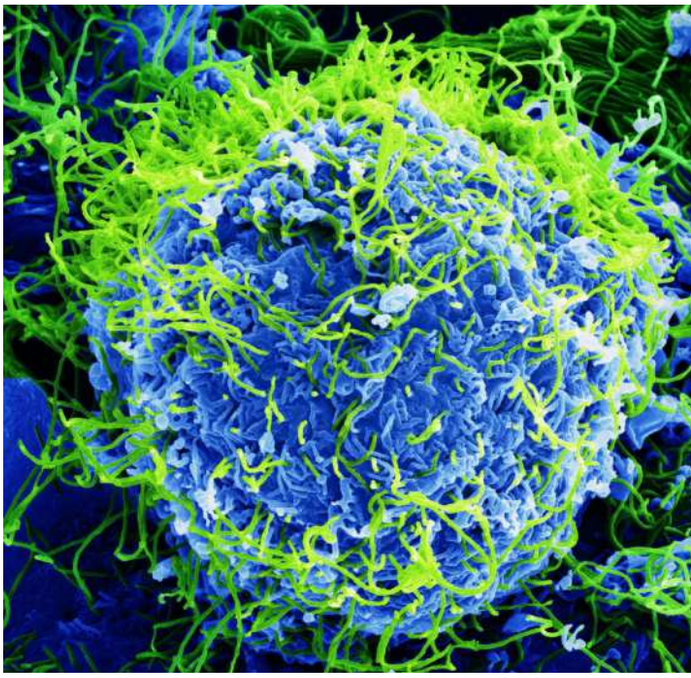
THE REGRESSION HYPOTHESIS

Viruses that exist today all gain by damaging their hosts, but it may not have always been this way. Many species in nature exist in symbiotic relationships, where both parties can benefit from the other's presence. An example of this would be the exchange of nutrients between fungi and plant roots in the soil, or African birds such as piapiacs that eat lice from the backs of large land mammals. Viruses may have once enjoyed such a mutually beneficial relationship with another organism. Over time, however, the viruses that decided to lose their own molecular machinery in favour of using their partner's could have gained an adaptive advantage. Making molecular apparatus is costly for a cell; it requires lots of genetic instructions, lots of energy and lots of resources. The viruses that accidentally lost these once-essential pieces of kit may have found that they could persist much better by instead using another's tools.

Although all known viruses today are obligate parasites, some larger viruses offer support for



Unlike viruses, single-celled organisms such as bacteria transcribe and translate their own genetic information



the regression hypothesis by resembling self-sufficient ancestors. The Mimivirus, for example, is a behemoth among viruses. Relative to other viruses, it is gargantuan in both how much genetic code it carries and simply how large it is. Adeno-associated viruses can be absolutely miniscule, measuring just 20 nanometres in diameter (that's 15,000-times smaller than a grain of salt!). They also have tiny lengths of genetic code containing just 4,500 nucleotide bases. In stark contrast, the giant Mimivirus can measure 500 nanometres and boasts a whopping genetic code of 1.2 million nucleotide bases. Not only does the size of the Mimivirus resemble fully living microbes, its DNA also contains instructions for an incomplete set of proteins responsible for metabolism and translation. Larger viruses also tend to depend on their hosts less than their smaller counterparts, with some being able to convert their DNA into RNA without direct input from the host. It has been proposed that these larger viruses, in particular the Mimivirus, could be examples of viruses that have retained many elements of what the ancestors of all viruses once possessed.

THE PROGRESSION HYPOTHESIS

Viruses straddle the boundary of what biologists consider to be life. On the one hand, they cannot regulate their internal state (a process known as homeostasis) or indeed carry out any metabolic processes, and independently they don't respond to stimuli. On the other hand, they do reproduce. This latter attribute is hugely important, because the ability to pass on genetic material is all that's needed for evolutionary processes to get to work. So the origin of viruses may not have arisen from an independent biological entity at all but from fragments of genetic code that became immensely effective at facilitating its own replication.

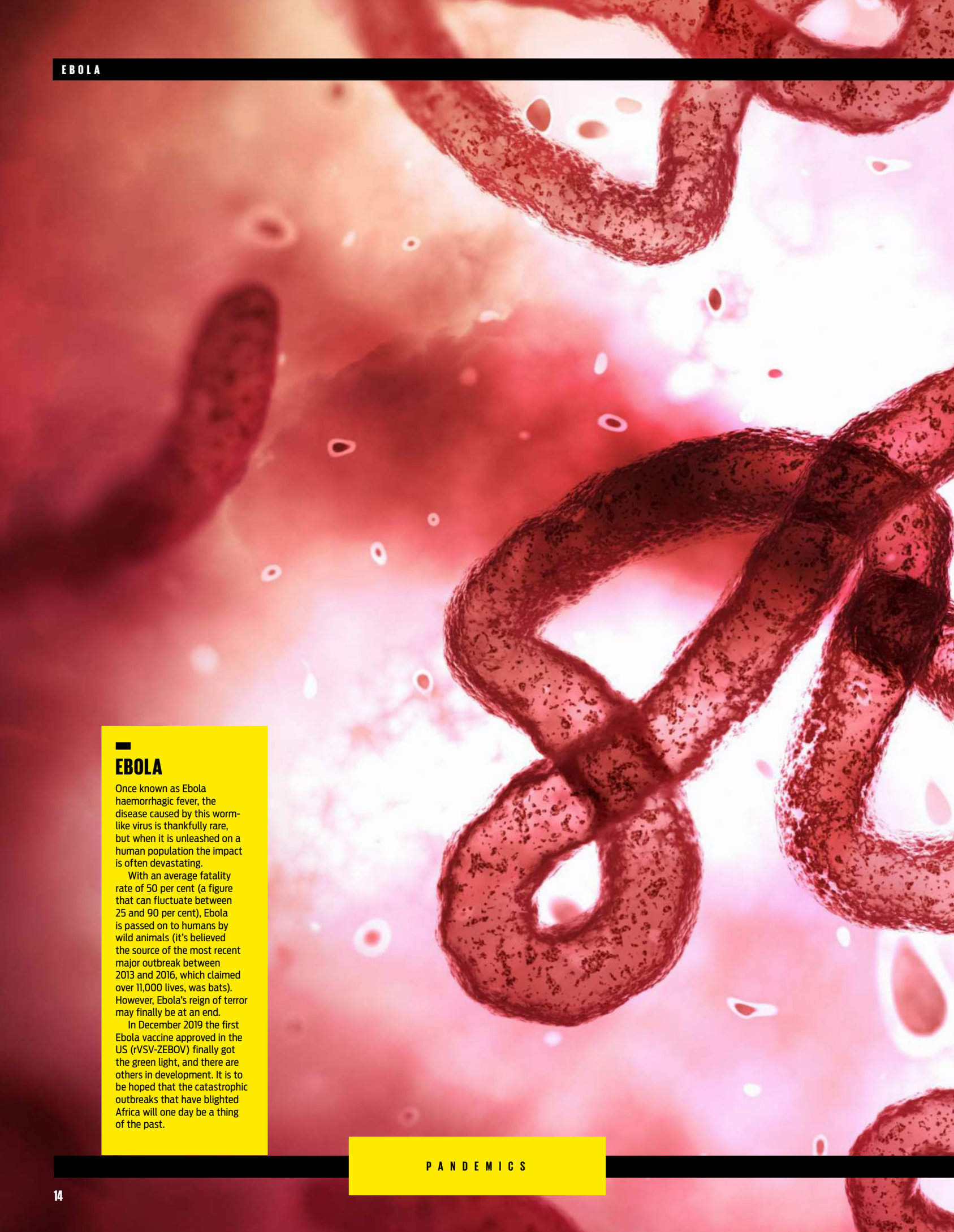
Transposable genetic elements are segments of genetic code that can move position within DNA. They are sometimes referred to as 'jumping genes' as they hop to either another location along the DNA strand or they jump to another strand of DNA entirely. The human genome is packed full of a form of jumping genes called retrotransposons. Retrotransposons can carry genetic instructions that allow them to be both copied and then pasted into new DNA, enabling them to be snugly integrated into the genetic fabric of a new cell. A family of viruses called retroviruses operates in a highly similar way, such as Human Immunodeficiency Viruses (HIV), which effectively infect and then integrate into their host's DNA. Proponents of the progression hypothesis recognise the familiarity between virus-like retrotransposons and retroviruses. What if a chance event gifted a retrotransposon new genetic material that allowed it to encase itself in a protein shell and easily migrate to new cells? The genetic code would not be alive, but it would be able to flourish and perhaps evolve into the viruses that exist in the world today.

CONCLUSION

The regression hypothesis argues that viruses are simple entities because they lost most of the molecular machinery needed to maintain life. The progression hypothesis instead argues that the first viruses never had this machinery to begin with but instead evolved from an assembled set of components needed for migrating and replicating genetic code. The precursor hypothesis, in contrast, suggests viruses lack complex cellular apparatus because they're remnants of an ancestral form of life that evolved before these units appeared.

Viruses are incredibly diverse entities. Some are tiny, others large; some possess DNA and others RNA. Depending on what group of viruses we zoom in on, certain theories seem more plausible. The gargantuan Mimivirus and other larger viruses like the Poxvirus are indicative of the regression hypothesis, retroviruses such as HIV the progressive hypothesis, and other RNA viruses the precursor hypothesis. One or all of these hypotheses may be correct. It is possible that rather than originating from a universal ancestor, viruses evolved multiple times independently. If this is the case, their shared features may be a product of a phenomenon known as convergent evolution, where natural selection causes different organisms to acquire the same trait. An example of this would be wings. Birds and insects haven't shared a common ancestor for millions of years, yet both converged on the same trait of flight.

If viruses in fact have multiple origins, then they may have picked up similar features through their shared 'lifestyles' of being obligate intracellular parasites. Alternatively, an as-yet unconsidered hypothesis may hold the answer, and only by continuing the search to discover new viruses will we discover the true origin of these fascinating biological entities.

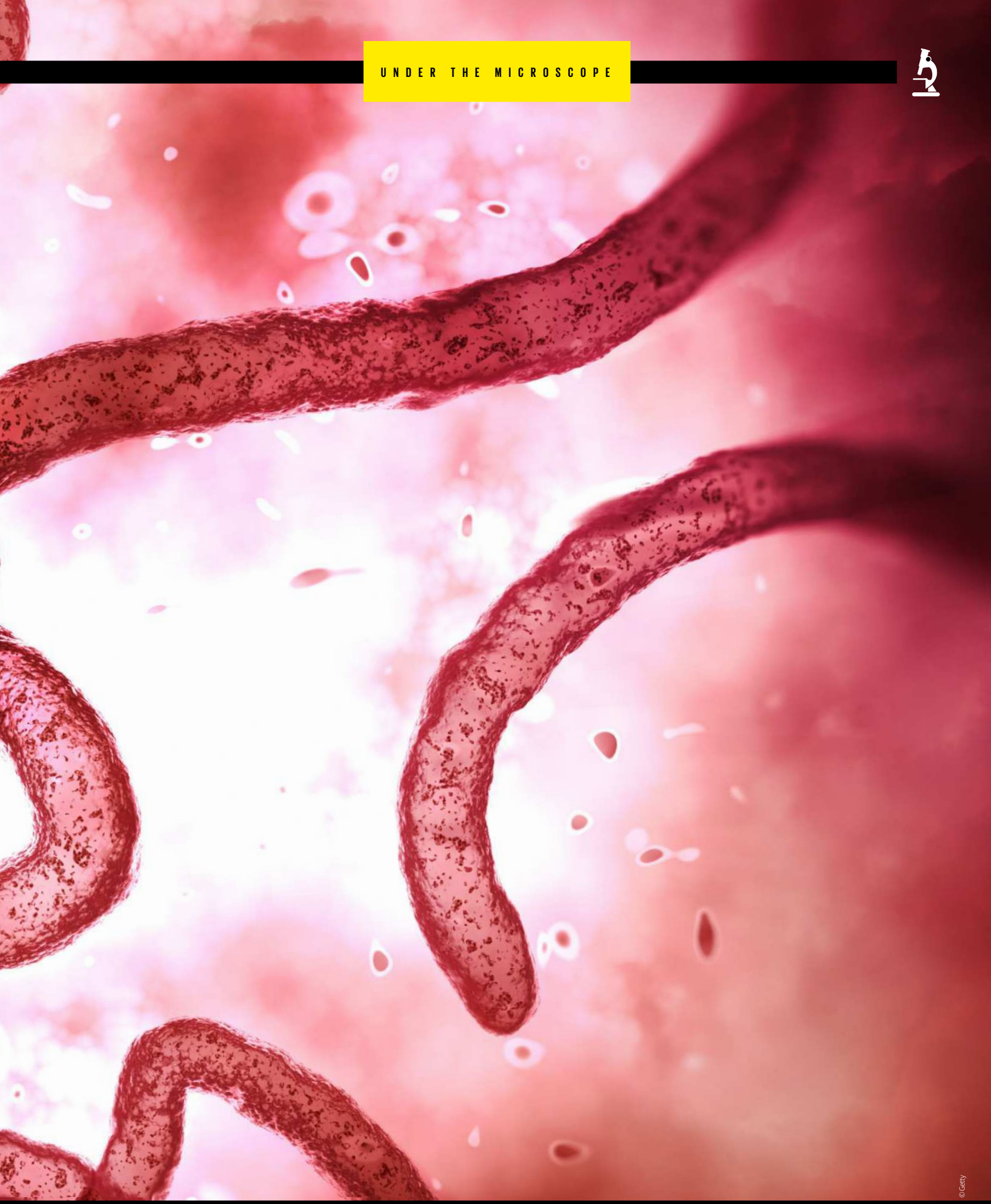


EBOLA

Once known as Ebola haemorrhagic fever, the disease caused by this worm-like virus is thankfully rare, but when it is unleashed on a human population the impact is often devastating.

With an average fatality rate of 50 per cent (a figure that can fluctuate between 25 and 90 per cent), Ebola is passed on to humans by wild animals (it's believed the source of the most recent major outbreak between 2013 and 2016, which claimed over 11,000 lives, was bats). However, Ebola's reign of terror may finally be at an end.

In December 2019 the first Ebola vaccine approved in the US (rVSV-ZEBOV) finally got the green light, and there are others in development. It is to be hoped that the catastrophic outbreaks that have blighted Africa will one day be a thing of the past.



HISTORIC PANDEMICS

OVER MILLENNIA, EPIDEMICS AND PANDEMICS HAVE KILLED MILLIONS ALL OVER THE WORLD, EVEN CONTRIBUTING TO THE DOWNFALL OF POWERFUL CIVILISATIONS

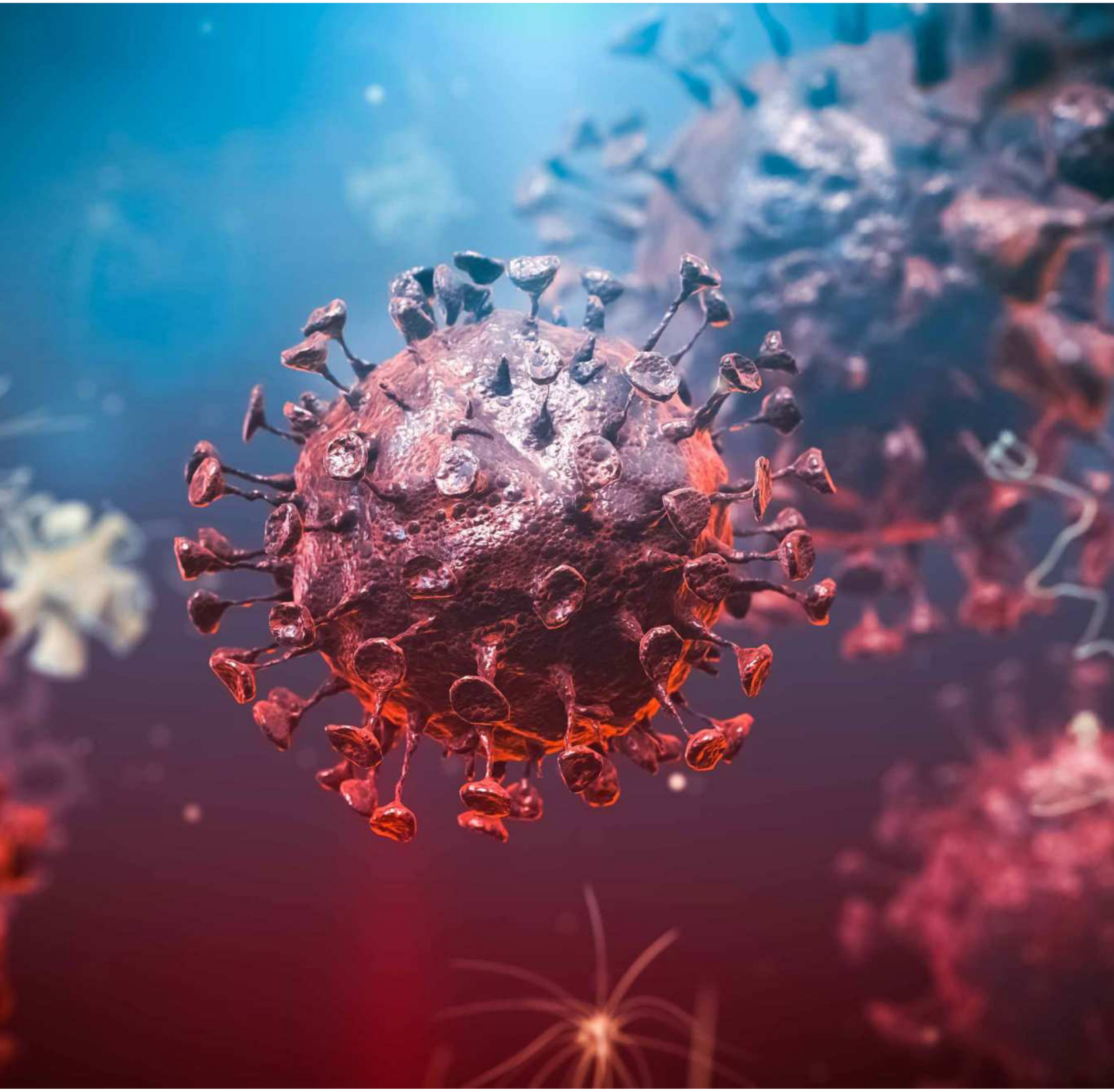
WRITTEN BY **BALJEET PANESAR**

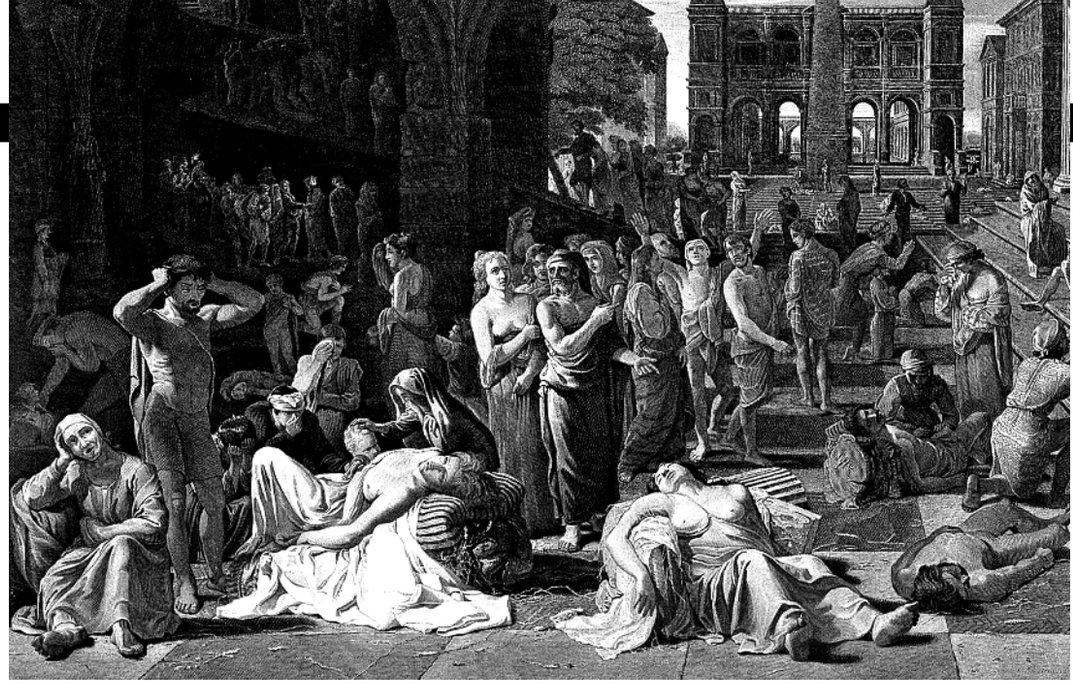
Diseases have ravaged humanity since ancient times; 5,000 years ago, an epidemic wiped out a village in China, and 3,000-year-old Egyptian mummies show the signs of smallpox. As humans have spread across the world, infectious diseases have spread too; nothing has killed more humans than disease-causing bacteria and viruses.

In prehistoric times, outbreaks of disease would be confined to one community. However, once trade and commerce allowed humans to interact with different animals, ecosystems and populations, it became much easier for diseases to spread and conquer the world. The Plague of Justinian, for example, spread across the Byzantine Empire's trade route through Asia, North Africa, Arabia and Europe and perhaps helped to initiate the downfall of this ancient civilisation, thereby changing the course of world history.

Between pandemics, humans have battled against measles, smallpox, influenza and polio, diseases that have killed millions of people over hundreds of years. Only smallpox has been eradicated – the others are still with us today.

Typically, over the last few hundred years pandemics have struck humans every ten to 50 years. Over more recent years, however, they have become more frequent and more deadly and are spreading more quickly.





1

LOCATION
Athens, Greece

DATE
430 BCE

DEATH TOLL
75,000-100,000

OUTBREAK

PLAGUE OF ATHENS

More than 2,400 years ago, as the cities of Athens and Sparta were battling in the Peloponnesian War, a deadly illness ripped through Athens, striking fear and panic into her citizens. The disease reached Athens via the port city of Piraeus, killing almost a third of its population, spreading throughout Greece and the eastern Mediterranean.

To protect the people of Athens, its leader, Pericles, ordered the Athenians to move within the city's newly built 'long walls', but this gave the disease the perfect conditions in which to thrive and quickly infect more of the Athenian population.

In *History Of The Peloponnesian War*, the ancient Greek historian Thucydides, who fell victim to the disease and survived, wrote that "people in good health were all of a sudden attacked by violent heats in the head, and redness and inflammation in the eyes, the inward parts, such as the throat or tongue, becoming bloody and emitted an unnatural and fetid breath". Despite written evidence of the disease its cause isn't known, though typhoid fever and Ebola are possibilities.

Months later, the disease finally subsided and for a brief period the Athenians were granted clemency, but it would strike twice more, forcing Athens to surrender to Sparta in 404 BCE and ending Athens' domination in ancient Greece.

2

LOCATION
Roman Empire

DATE
165–180 CE

DEATH TOLL
5,000,000

OUTBREAK

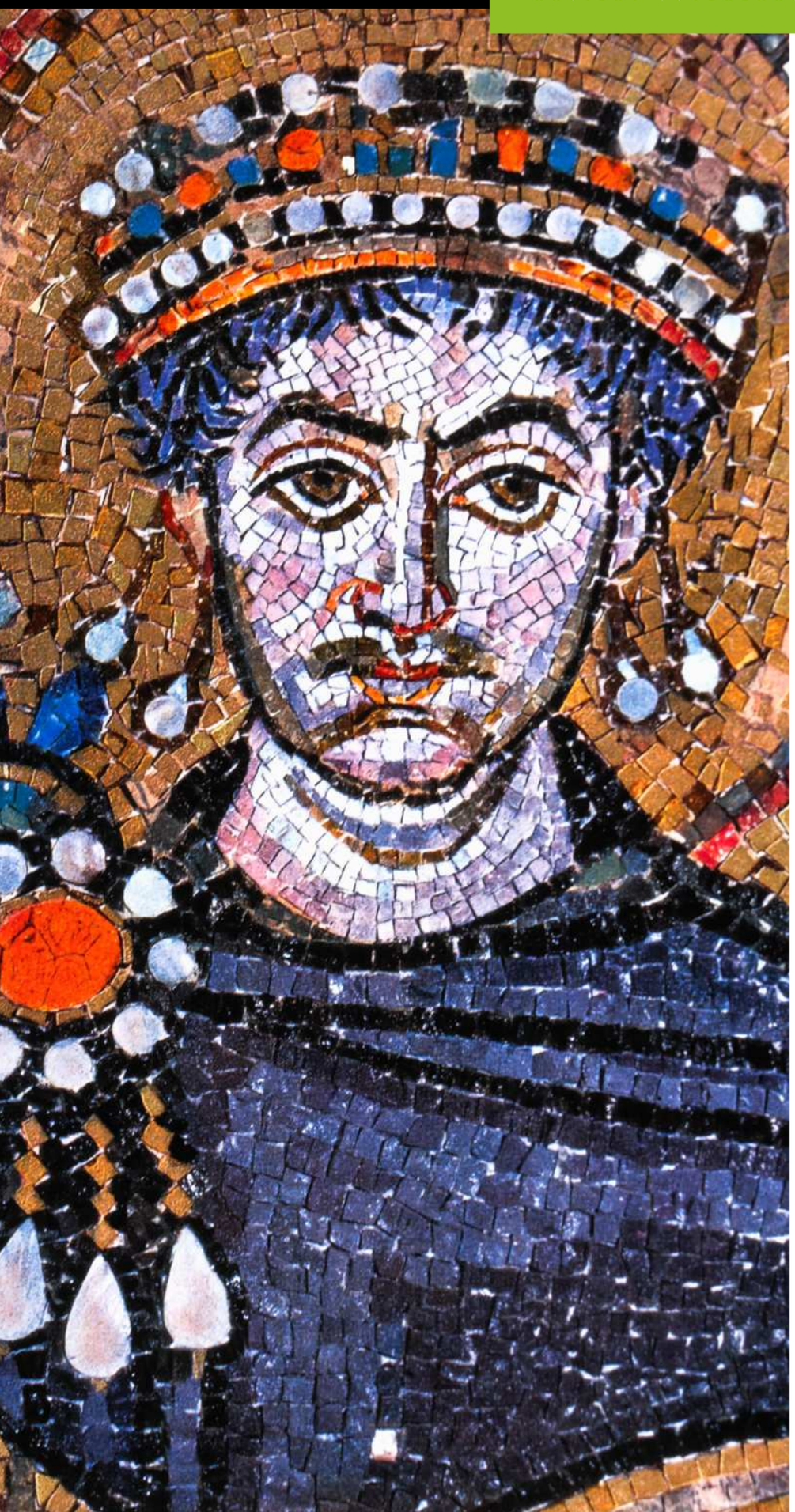
ANTONINE PLAGUE

A gruesome and disfiguring disease named after the Roman Emperor Marcus Aurelius Antoninus was brought to Rome at the height of the Roman Empire. As soldiers returned from battle in the Near East, they brought home more than just pride and victory. Once they reached Rome, there was no stopping the disease and it spread throughout Europe, having already raced across Asia Minor, Greece and Italy.

The disease caused fevers, chills, black diarrhoea and red and black papules on skin, which caused severe scarring after they had scabbed – a sign that their bearer had survived the disease. For two to three weeks victims would suffer until they could fight no longer. Victims would first experience symptoms two weeks after being infected, a feature that allowed it to spread rapidly all over the empire. The disease was probably smallpox, and it was documented by the Greek doctor Galen.

Up to 2,000 people were killed per day, a fate that awaited some ten per cent of the empire's soldiers, but in some places up to a third of the Roman population would perish, decimating the empire's army. In response, all offensive campaigns were postponed – there were not enough men to fight. Eventually, freed slaves, gladiators and criminals – who normally would not qualify for military service – were recruited after Germanic tribes began to claim more of the Roman Empire's territory.

Over the next two decades the empire would experience two more outbreaks, ultimately contributing to the downfall of one of the world's largest ever empires.



3

LOCATION
Byzantine Empire

DATE
541–542 CE

DEATH TOLL
25,000,000+

OUTBREAK

PLAGUE OF JUSTINIAN

By 540 CE, the Byzantine Empire had conquered most of Italy and North Africa. Spain was next on the list. But the following year, a new disease would emerge in the port city of Pelusium, Egypt, and devastate the Byzantine capital of Constantinople (modern-day Istanbul, Turkey). This disease – the bubonic plague – would kill millions of people as it spread through the vast empire and marked the start of the decline of one of the greatest empires in history.

Named after the Byzantine Emperor Justinian I, the Plague of Justinian is the first known of the three deadly plague pandemics, caused by the bacteria *Yersinia pestis*. As a tribute to the emperor's powerful realm, ships carrying grain and cloth were sent to Constantinople from North Africa. However, these ships also carried flea-infested rats that would infect people with plague throughout Asia, Arabia, North Africa and Europe.

Victims of the disease would develop a fever and black, pus-filled blisters called buboes. Some victims would become delusional and paranoid. In a matter of days the victim would perish; in Constantinople, the contagion would kill 5,000 people each day, and in time around 40 per cent of the city's population. Even the emperor was infected, but he survived. Further outbreaks ravaged the Mediterranean Basin and Europe for more than 200 years, resulting in the deaths of half of Europe's population despite the disease becoming less deadly with each outbreak. The disease would finally disappear in 750 CE.

4

LOCATION
Mexico

DATE
1545–1548

DEATH TOLL
15,000,000

OUTBREAK

COCOLIZTLI EPIDEMIC

Following the arrival of Europeans in present-day Mexico, one of the deadliest epidemics in human history struck the Aztecs. The Aztecs were vulnerable; the Europeans had brought disease from their faraway lands that the Aztecs had never encountered and had no immunity against. Of the three epidemics that ravaged Mexico during the 16th century, it was the second outbreak that would be the most devastating, wiping out up to 80 per cent of the indigenous population.

The natives named the mysterious disease 'cocoliztli', which means 'pestilence' in the local Nahuatl language. The disease caused fevers, hallucinations and bleeding from the eyes, mouth and nose. Victims would succumb to the disease between three and four days after infection. Hundreds of people perished each day.

For 500 years the cause of the epidemic had been unknown, but a recent study found that a rare strain of salmonella called Salmonella paratyphi C may have been responsible. The bacteria are known to cause enteric fevers in humans, for example typhoid, but this strain of salmonella seldom causes disease in humans today.

5

OUTBREAK

GREAT PLAGUE OF MARSEILLE

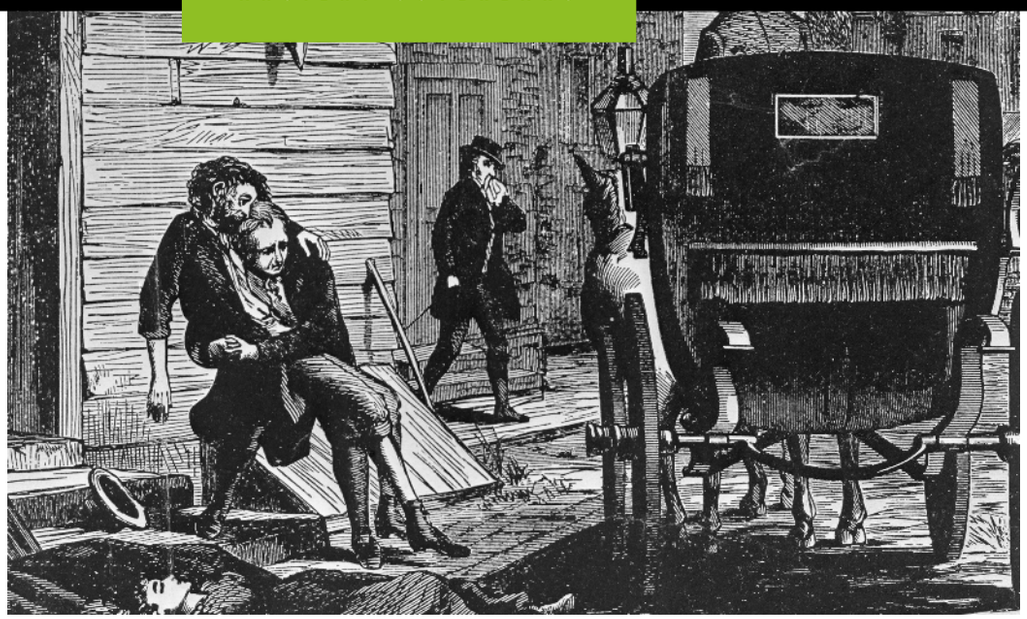
After travelling in the eastern Mediterranean for about a year, a ship called the Grand Saint-Antoine arrived at its final destination, the port city of Marseille. Its cargo of silk and cotton was destined for a trade show, but hidden among the luxurious goods was the bacteria *Yersinia pestis*, which would soon be responsible for the Great Plague of Marseille. During the voyage, several men had died on board, including a passenger who perished two months before the ship's arrival in Marseille. Despite the signs of bubonic plague on the ship, it was only quarantined for a few days, resulting in Western Europe's last major outbreak of bubonic plague.

Within days of arriving in Marseille, the disease claimed its first victims. Corruption, negligence and misinformation all contributed to the spread of the disease; officials even paid doctors to diagnose the disease as pestilential fever, not plague. Only two months later, once the disease could no longer be contained, were measures taken to reduce the spread of the epidemic. These included stopping trade, quarantining people, burying corpses and disinfecting the city. As for the fate of the Grand Saint-Antoine? The ship was burned off the coast of Marseille.

LOCATION
Marseille, France

DATE
1720–1723

DEATH TOLL
100,000



6

OUTBREAK

PHILADELPHIA YELLOW FEVER EPIDEMIC

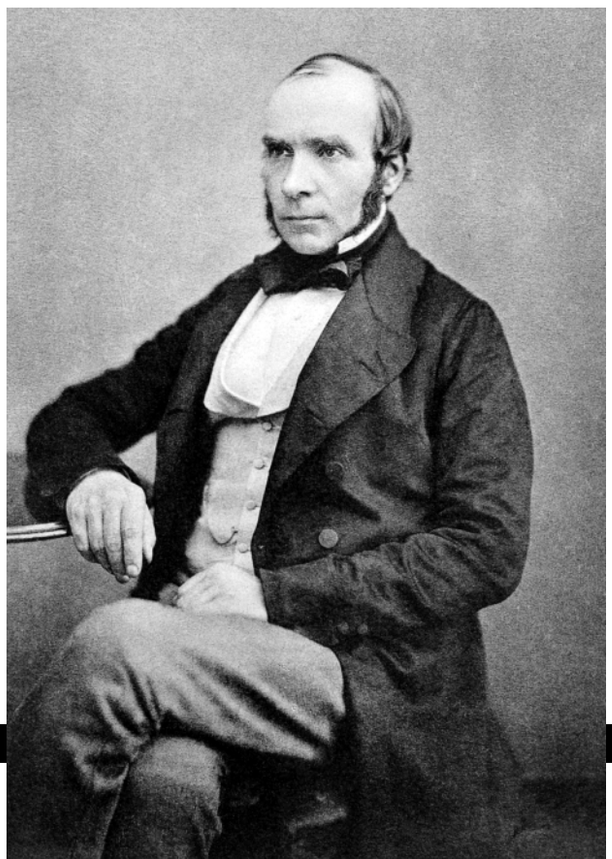
LOCATION
Philadelphia, US

DATE
1793

DEATH TOLL
5,000

The summer of 1793 was particularly hot and humid in the city of Philadelphia – then the largest city in the US and the nation's capital. It would be a summer that no one would forget. Over the course of four months, a disease that caused fevers, chills, jaundice and bleeding from the mouth, nose, eyes and stomach ravaged the city, claiming the lives of ten per cent of its population. The disease was yellow fever, and it was one of the worst outbreaks ever recorded in US history. As the mysterious disease spread through the city, 20,000 people – about half of the city's population – fled, including President George Washington. Philadelphia's most prominent doctor, Dr Benjamin Rush, stayed. He believed that yellow fever was caused by the city's polluted air and unsanitary conditions. Scientists would not discover that the deadly disease was transmitted by mosquitoes until a century later.

At the height of the epidemic more than 100 people succumbed to the disease every day; towards the end of the epidemic, the death toll fell to about 20 per day. Eventually frost ended this epidemic by killing the mosquitoes. Today, an effective vaccine stops most people from getting yellow fever, which still claims the lives of around 30,000 people each year globally.



7

OUTBREAK

THIRD CHOLERA OUTBREAK

LOCATION
Worldwide

DATE
1852–1860

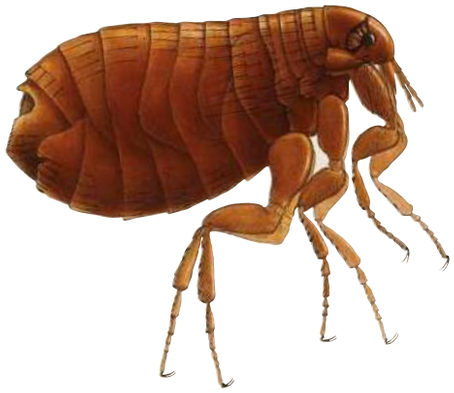
DEATH TOLL
1,000,000+

In the past 200 years there have been seven major outbreaks of cholera around the world. The deadliest was the third outbreak, which decimated populations in Africa, Asia, Europe and North America. The disease was caused by the bacteria *Vibrio cholerae*, which spread via contaminated food and water. The infection would cause dehydration and diarrhoea, killing its victims within hours.

The outbreak is thought to have originated in India and was initially spread across Asia by soldiers. As they marched across Asia they carried the disease into Afghanistan, resulting in the deaths of hundreds of thousands of people. At the height of the British Empire, trade ships would spread the contagion across Arabia. Once Russia was infected, the disease would spread quickly, resulting in the deaths of 1 million people.

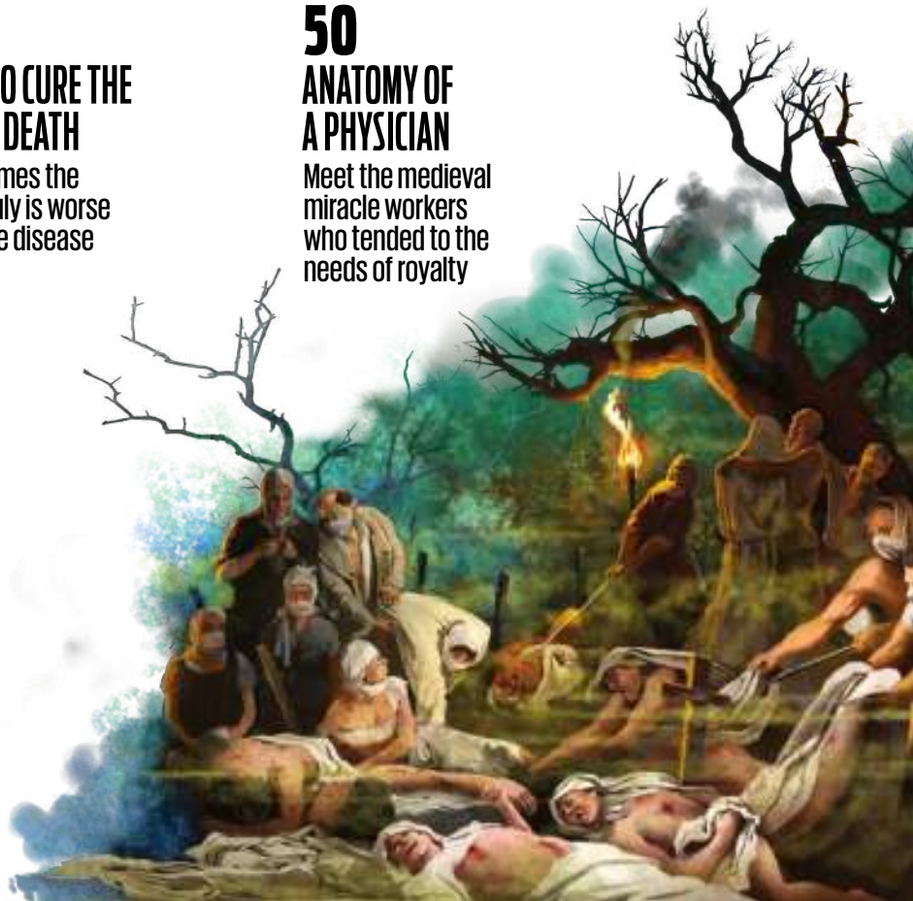
In 1854 cholera hit London, killing more than 150 people in just three days. An English doctor named John Snow had lived through previous cholera outbreaks and had a theory that somehow contaminated water caused the disease. He was right. He figured out that a water pump was the source, and eventually it was shut down. Cholera cases decreased immediately. His work would radically change attitudes to public health.

Cholera, however, is still a daily threat to billions of people around the world. Each year there are 1.3 to 4 million cases of cholera and between 21,000 and 143,000 deaths.



THE BLACK

DEATH



HISTORY OF THE BLACK DEATH

THE TERRIFYING TRUE STORY OF THE OUTBREAK THAT CRIPPLED THE WORLD

WRITTEN BY **GAVIN THOMAS**

After enjoying generations of sunshine and warmer climes, Europe had undergone an unprecedented population boom that saw more people living on the continent than ever before. At the turn of the first millennium there were 24 million people in Europe. By 1340 the continent's population had boomed to 54 million.

Entire countries were straining at the edges of their farmlands and eating into the forests, and the availability of food was beginning to reach the limits of population support. A dire evil, however, stalked the land, just as the Little Ice Age began, and a century later Europe's population had plummeted to 37 million.

The true origins of this bringer of death are unknown, though many people believe it emerged in southeast Africa centuries ago and crept along the Nile to the Eurasian continent. This monster scurried on a million legs through the dank holds of ships, grain-stuffed silos and mills, filthy streets and docks slick with grime – and much worse in the years to come.

It sprang from the backs of great black rats, borne in the blood of fleas infected with *Yersinia pestis*, and thrived in the blood-flecked sputum of the plague's violently coughing victims. It wept from the bulbous, stinking sores that erupted in people's groins and armpits. It struck fiercely and mercilessly, bringing down towns in a matter of days, erasing families in mere hours.

While we now call this great pandemic that brought Europe to its knees in the mid-14th century the Black Death, it was known by a different name at the time – the apocalyptic moniker pestilence. With the Hundred Years' War sweeping Western Europe and conflicts with the unstoppable Golden Horde in the east, famine beginning to cripple countries whose populations were at the limits of sustainability, and then sickness swiftly following – bringing with it death – the people of the world knew that pestilence was upon them, and many feared the apocalypse was looming.

Pestilence is shrouded in mystery, and even now researchers still debate the exact components of the beast and the path it took across the continent. What is certain is that it originated in the eastern end of the continent and worked its way through the Mongol Empire before piercing Caffa (now Feodosiya in Ukraine), Sicily and southern Europe, reaching peak strength as it smashed into France and England.

Scientists agree that its main weapon was bubonic plague, a bacterial disease carried by infected fleas that fed on the black rats ubiquitous to the continent but were also known to dine on other types of rodents, rabbits and sometimes larger mammals like cats.

The bacteria itself – *Yersinia pestis* – was a rather nasty piece of work; it would infect the blood of fleas and then cause a build-up of old blood and cells within the proventriculus (a valve preceding the flea's stomach). This blockage meant that when a hungry flea tried to bite its next victim, the high pressure in its stomach would force some of the ingested

blood back out into the open wound, along with thousands of bacterial cells that had accumulated in the proventriculus.

This swarm of *Yersinia pestis* would then drain along the lymphatic tract of the victim from the source of the bite down to the nearest lymph node. Once there, the bacteria would proceed to colonise the lymph node so entirely that it would swell, stiffen and ooze a rancid pus. Since most people were bitten on their legs, this would usually be the lymph node in the groin. These enlarged lymph nodes, known as buboes, were the main sign of pestilence; ugly and painful, they ranged from the size of a grape to a fat orange and they made any kind of movement completely unbearable.

Before the appearance of the buboes, though, victims would have a slight warning. Flu-like symptoms would appear first, swiftly followed by a high fever. Within a day or two these would be joined by 'God's tokens' – small, circular rashes, also called roses – that would spread over the body and particularly around infected lymph nodes. Caused by weak blood vessel walls and internal haemorrhaging, they were a sure sign that you didn't just have a nasty cold, as noted by Shakespeare: "The tokened pestilence where death is sure." Things tended to move quickly once the buboes had boiled up through the skin. Diarrhoea and vomiting would ensue, as would septic shock due to the buboes bursting, with respiratory failure and pneumonia wiping up the last sops of life. Within two weeks, four out of five people who contracted the plague died.

Agnolo di Tura del Grasso, a chronicler from Siena in central Italy, captured the terror of the time well. "I do not know where to begin describing its relentless cruelty; almost everyone who witnessed it seemed stupefied by grief. It is not possible for the human tongue to recount such a horrible thing, and those who did not see such horrors can well be called blessed. They died almost immediately; they would swell up under the armpits and in the groin and drop dead while talking. Fathers abandoned their children, wives left their husbands, brothers forsook each other; all fled from each other because it seemed that the disease could be passed on by breath and sight. And so they died, and one could not find people to carry out burials for money or friendship."

In the face of pestilence and the approaching end-times, King Philip VI of France commissioned the Faculty of Medicine at the University of Paris to deduce the source of the evil so that it might be eradicated. The findings of these professors did not bode well, for they ascribed the tragedy to the conjunction of Saturn, Mars and Jupiter in Aquarius, and to the position of Saturn in the House of Jupiter – and nothing could be done to challenge the will of the cosmos. At the time, Jupiter was believed to be the source of warm, humid vapours, while hot, dry Mars was thought to ignite them. These pestilential vapours were thought to form a thick, stinking smog of sickness known as a miasma, which was compounded by the sulphurous eruptions of volcanoes and the wrathful power of earthquakes.

Believed to be the main culprit of the Black Death, people gave up bathing (as it opened the pores to miasma), barricaded themselves in closed rooms hung with thick tapestries to block out the poisoned air and took to carrying nosegays and pomanders to avail themselves of the evil stench. None of these measures would save them though.

In 1346, amid reports from the east of biblical plagues – rains of frogs and serpents, hail, stinking smoke and thunder – the Mongols of the Golden Horde attacked Caffa, an island port off the north coast of the Black Sea. The horde laid siege to the city and were all set for a protracted campaign when the Black Death tore through their ranks. Suddenly, their army was dying, and the siege began to fall apart. What followed is the first known incidence of biological warfare: about to pull back and return to the east, the horde first gathered up the diseased bodies of their dead and catapulted them over the walls of Caffa.

Instantly, pestilence struck Europe, and though it took around 15 years to cross Asia it would destroy Europe in less than five. As the horde went home, defeated, the Black Death ran around the coast of the Black Sea and straight through the Byzantine Empire (south of modern Bulgaria). By 1347 – just as Joan of England, of the House Plantagenet, was departing Britain to marry Prince Pedro of Castile and form a political alliance – it had arrived on the Mediterranean and struck Messina in Sicily. Here, frightened peasants were beginning to realise that the monster attacked by sea and so had started to refuse ships at the port, but it was a case of too little, too late.

Trading ships from Genova and Constantinople carried the plague to the Italian mainland, where it rippled along rivers, canals and walkways. By 1348, 600 people were dying each day in Venice; Rhodes, Cyprus and Messina had all fallen. The invasion gathered pace and then punched up into the heart of Europe, striking down 60 per cent of Marseille's population and half of Paris'. The bewildering death toll was so high the mayor of Bordeaux even set fire to the port, a remarkably prescient move considering the fact that serpents and smog were more feared than rats at this stage.

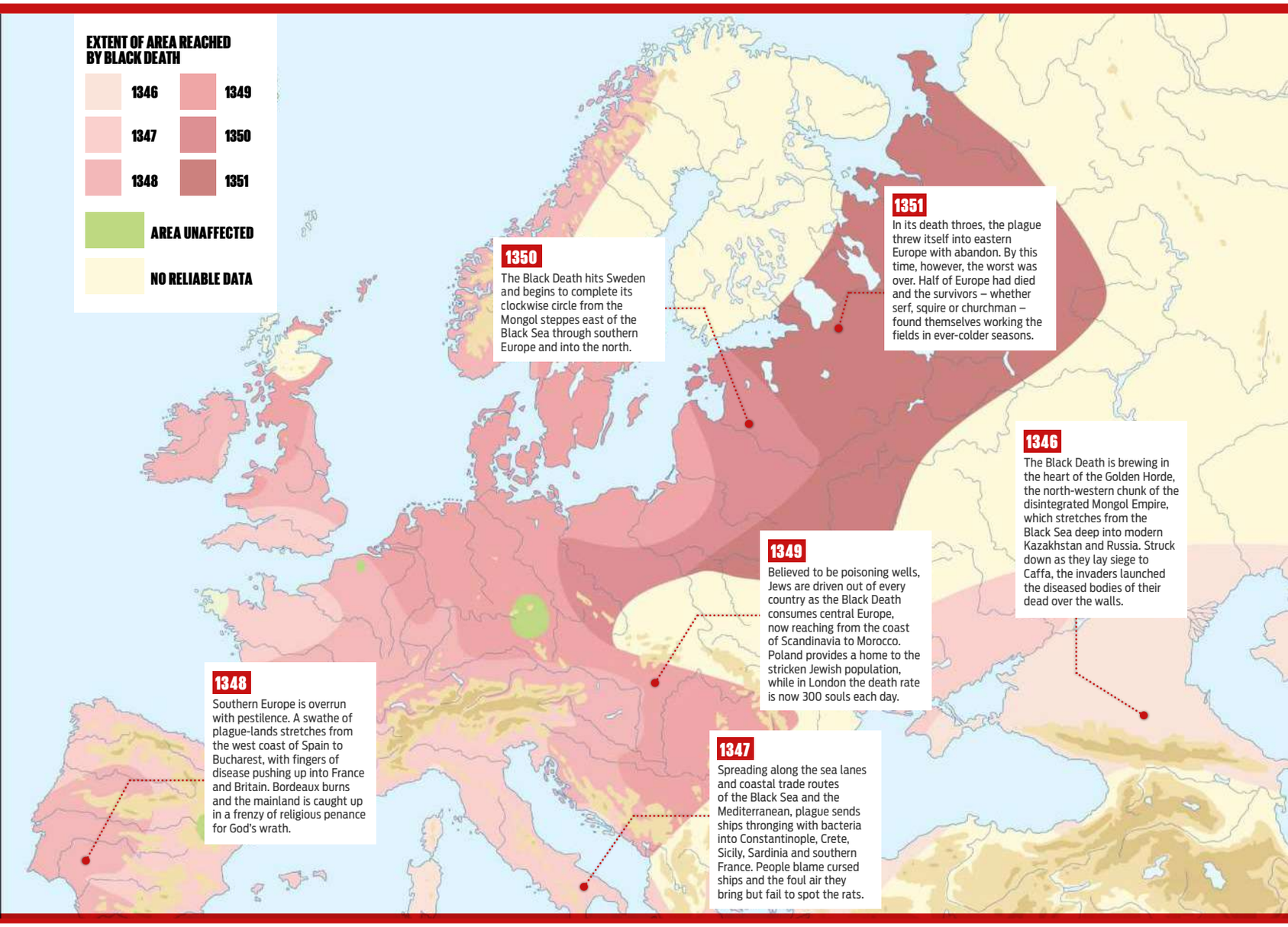
Britain fared little better at the time. Arriving on the south coast of England in 1348 – primarily

KILL OR CURE

A number of herbal treatments were thought to be effective against the Black Death. Sufferers were regularly prescribed solutions of ground emeralds or potions made from the crushed shells of newly laid eggs mixed with chopped marigolds, ale and treacle. Treacle was a leading remedy, though it had to be at least ten years old to have any potency. Another effective – if less appealing – curative was urine. Drinking two glasses a day was widely thought to strengthen the constitution.

Treatment of the buboes was a trickier affair. In their terror, people believed they could draw out pestilence by holding bread against the boils and burying it – or, more incredibly, by strapping a live hen to the swelling, rinsing and repeating. Physicians later discovered that lancing buboes, draining the pus and applying poultices was relatively effective in the affliction's early stages. Such poultices usually consisted of tree resin, white lily root and then dried human excrement, arsenic or dried toad, depending on availability. Less extreme ointments were mixed from cooked onions, butter and garlic, while bloodletting through leeches or surgical incisions and the application of clay and violets was also practised.

For the most part, since the Black Death was allegedly miasmatic, the best preventative measure was thought to be carrying pouches of sweet herbs and spices (or balls of perfume called pomanders) and burning them in your home. Most felt their only options were to fast, pray and join the Flagellants in order to pay penance for their sins and kill suspected witches or well-poisoners while waiting for Saturn to move out of the House of Jupiter.



1350
The Black Death hits Sweden and begins to complete its clockwise circle from the Mongol steppes east of the Black Sea through southern Europe and into the north.

1351
In its death throes, the plague threw itself into eastern Europe with abandon. By this time, however, the worst was over. Half of Europe had died and the survivors – whether serf, squire or churchman – found themselves working the fields in ever-colder seasons.

1346
The Black Death is brewing in the heart of the Golden Horde, the north-western chunk of the disintegrated Mongol Empire, which stretches from the Black Sea deep into modern Kazakhstan and Russia. Struck down as they lay siege to Caffa, the invaders launched the diseased bodies of their dead over the walls.

1349
Believed to be poisoning wells, Jews are driven out of every country as the Black Death consumes central Europe, now reaching from the coast of Scandinavia to Morocco. Poland provides a home to the stricken Jewish population, while in London the death rate is now 300 souls each day.

1348
Southern Europe is overrun with pestilence. A swathe of plague-lands stretches from the west coast of Spain to Bucharest, with fingers of disease pushing up into France and Britain. Bordeaux burns and the mainland is caught up in a frenzy of religious penance for God's wrath.

1347
Spreading along the sea lanes and coastal trade routes of the Black Sea and the Mediterranean, plague sends ships thronging with bacteria into Constantinople, Crete, Sicily, Sardinia and southern France. People blame cursed ships and the foul air they bring but fail to spot the rats.

WHEN PESTILENCE STRIKES...

FLU HITS
The Black Death begins like a bad cold, with aches, pains, chills and a fever setting in.

GOD'S TOKENS
Just a few hours later, circular red rashes appear around infected lymph nodes.

BUBO BREAKOUT
Within a day or two, the lymph nodes blacken and swell to the size of oranges.

VOMITING
Severe fluid loss, including blood, accompanies and exacerbates the bloating buboes.

SEPTIC SHOCK
Two to three days after infection, septic shock and pneumonia often hit the victim.

RESPIRATORY FAILURE
Weakened under the assault, the body's central systems begin to shut down.

DEATH
Usually within two to four days, pestilence conquers the host.

A French painting of plague sufferers being tended to outside a temple

through ports like Bristol, Weymouth and London – the Black Death was to claim 50 per cent of the population and reach a height of taking around 300 souls each day in London by spring 1349.

It was a staggering loss in this age of arable farming, where the majority of the country's wealth lay in the land. Acres and acres of golden cornfields were left without farmers to sow or plough them; knights and churchmen found themselves working by the sweat of their brows, and this led to the growth of the new yeoman class, as serf-less landowners were forced to rent their estates to the surviving farmers, whose labour was now very much in demand against crippling inflation and who became independent for the first time. This freed up capital and made it more economically mobile, possibly leading to the birth of a kind of proto-capitalism, but it also led to the English 'lost villages'.

As well as being depopulated through disease, the estates of the rich also succumbed to the fat dowers of widows who were entitled, for life, to a third of their dead spouse's income. With the death rate increasing and ageing spinsters gobbling up inheritances, young lords were as out of pocket as the poor and stood no better chance against pestilence. While the chronic overpopulation in England before the Black Death meant that there was no initial effect on the labour market, by the next generation – the 1370s – there was a critical shortage. This led to the British Government passing increasingly stringent regulations aimed at holding down rising wages and ultimately to the Peasants' Revolt of 1381. The same was true elsewhere in Europe, with the effects of the Black Death also leading to the Jacquerie in France (1358) and the Revolt of the Ciompi in Italy (1378).

Despite the reassurance that the clergy provided, religion was powerless against the Black Death. Churchmen, who were often the closest thing to a doctor, were forbidden to dissect the bodies of God and so could not perform autopsies to learn the exact causes of death. Priests afraid of the plague refused to administer last rites and urged people to confess to each other. Funeral rites were similarly abandoned, with corpses stacked several layers deep with a smattering of earth between each row, and entrepreneurial peasants began to gather and bury the dead for a fee.

"THE PLAGUE HAD CLAIMED AN ESTIMATED 40-50 PER CENT OF THE EUROPEAN POPULATION – THAT'S AROUND 20 MILLION PEOPLE"

Eventually, the clergy refused bodies entry into cities and, since death had become such a constant companion, ordained that no funeral bells were to ring. In 1348, however, a much greater religious threat abounded. The Brotherhood of Flagellants rose up in Germany and led 1,000-strong marches through the country for 33 and a half days at a time (to mark the Saviour's years on Earth), brutally whipping themselves with iron-studded belts of leather to display their penance to God and earn protection from his wrath. They had something of a rock-star status, and many people reached out to catch the sacred drops of blood that spattered from their holy wounds.

By 1349 the movement had petered out, falling prey to a bandwagon effect that led to too many misfits and vagabonds exploiting the Flagellants' notoriety, but the effect it had on public sentiment was grave. The reinforcement

of extreme Christian ideology in the face of the apocalypse inflamed anti-Semitism across Europe, and Jewish populations were persecuted like never before.

Associated as they were with the mystical Kabbalah (and black magic), the 2.5 million Jews living in Europe at the time were prime suspects for witchcraft and nefarious deeds. Having been strong international merchants in the year 1000, they were in a period of decline that would ultimately lead to their replacement in economic terms by Italian merchants by 1500. Divided and wandering across Europe, they were accused of brewing poisons from basilisk skin, spiders, lizards and frogs – even Christian hearts and the wafer of Christ – and then deliberately infecting wells with disease.

False confessions under torture, such as that of Agimet the Jew during the plague's peak in 1348, certainly didn't help matters, and on Valentine's Day of 1349 in Strasbourg 2,000 Jews were burned in a cemetery. The crime was repeated in other cities across Germany and Switzerland, prompting a mass Jewish migration across Europe.

It was to Poland that they fled, as King Casimir was in love with a Jewish woman and so opened the borders of his country to his lover's kinsmen, where they would remain until the Holocaust. Yet while the Jews were fleeing death and destruction at the hands of humans, the monster itself was winding down. Pestilence reached Sweden in 1350 and, by the time it got to Russia, the plague had all but passed in France and England.

Historians have never reached complete agreement on what exactly stopped the disease, though quarantines, slightly better standards of hygiene and the reduced number of people travelling back and forth through Europe – as a result of mass depopulation and a growing fear of infective trade routes – are all thought to have played a role. The plague had claimed an estimated 40-50 per cent of the European population – that's around 20 million people. By way of comparison, the Spanish Flu that followed the end of WWI in 1918 – raging across a far more populous Europe – claimed 50 million lives. Never before or since has such a potent infection wracked the continent.

There is a nursery rhyme still sung today that is believed by some to bear the terrible mark of the plague, an unconscious testament to the deep psychological impact it had upon the survivors: 'Ring around the roses; a pocketful of posies; ashes, ashes; we all fall down!'. In the early stages of the plague, the afflicted were known to develop rosy red rashes on the skin in the shape of a ring, and 'posies' – nosegays of dried flowers, or small pouches of sweet-smelling herbs – were often carried to ward off the disease.

Unaware of the true nature of the monster, many believed the Black Death was a miasmatic illness, caused by noxious, pestilential fumes in the air. As such, posies were carried and incense burned in homes. People forwent bathing (as it opened the pores) and even splashed themselves in urine to bolster their natural protection against external fumes and vapours. It is thought that the first two lines of the rhyme refer to this.

As for the closing lines, historians believe that the Great Fire of London (1666) – which wiped out the black rats of the city – was the only thing that saved England from succumbing entirely. It took Europe 150 years to fully recover, and those who survived believed that they had witnessed the apocalypse.

With war, death and famine rampant in the century following the Black Death, it was as if the four horsemen themselves had ridden out in force to bring Europe to its knees. To a superstitious, God-fearing populace, it was a hell on Earth that they were utterly powerless to defend themselves against.

Funerals for plague victims would often be performed at night to limit contact with other people

LAZZARETTO ISLANDS

VENICE'S QUARANTINE STATIONS, 15TH CENTURY

The Black Death was spread from victim to victim through fleabites, body fluids and sometimes on the droplets of a cough or sneeze. This meant that major medieval cities, where the common people lived in cramped and dirty conditions, were a breeding ground for such infections. As commercial hubs, the cities and ports also attracted traders who would either bring the plague with them or catch it while visiting and pass it on as they travelled.

Though the exact cause of the Black Death and how it spread wasn't understood at the time, contemporary city burghers did what they could to isolate the sick. Infected houses were locked down, animals were banned from the streets, bodies were hauled into pits, public gatherings were forbidden and trade was halted.

In 1348, the Venetians came up with a grand plan to prevent the disease from spreading through their population: quarantine. Any vessel that wanted to enter the island city's ports had to spend 40 days anchored offshore to prove that its passengers were not sick – or die trying. In 1403, the citizens went one step further and built a public hospital on the neighbouring island of Lazzaretto Vecchio in order to isolate any citizens that showed signs of plague.

Considered a success, soon more islands in the Venetian Lagoon – like Lazzaretto Nuovo and Poveglia – were turned into holding pens for potential plague carriers. Rather than staying on their ships, newcomers were encouraged to maroon themselves on these islands while handing over their cargo to be 'decontaminated'. Meanwhile, the waters were guarded by armed patrols, and anyone who violated the rules was sent to the gallows.

While Venetians were able to curb the damage as the plague struck Europe, the reality was that being sent to one of these islands was often a death sentence. More than 1,500 skeletons have been unearthed on Lazzaretto Vecchio, and thousands more are thought to be lurking beneath the ground.

GUNPOWDER STORAGE

After the Black Death of 1346-53, plagues came and went across Europe, and between outbreaks the island was used to store gunpowder in two 'torresini da polvere'. This dangerous substance was unstable, so the quarantine islands provided the perfect location for storage away from the healthy population of Venice.

MASS GRAVE

At the height of the plagues of the 14th and 16th centuries, hundreds of people died every day on the islands and the body carriers were overwhelmed. The corpses were piled into mass graves, or plague pits, and it's rumoured that many were buried before they had even died.

DECONTAMINATION

Contemporary medicine believed that the plague was spread by miasma (bad air). In an attempt to tackle this, juniper, rosemary and other herbs were piled up and burnt. Soiled clothes were boiled or coated in vinegar, and the cargo from incoming ships was left in the open air to be 'decontaminated'.

UNSAFE HARBOUR

Plague victims were taken to the island by boat and left on their shores to protect the people of Venice from infection. Incoming ships were also made to wait on one of the islands in case their crew were carrying the disease. The word 'quarantine' comes from the Italian 'quarantina giorni', meaning 40 days – the time ships were made to wait before making port.

NOBLES' QUARTERS

The island's original facilities had the capacity to hold just over 200 people. Separate quarters were built to house those of higher social status, but the plague was indiscriminate, and once they succumbed to the disease they were buried alongside paupers in the same mass graves. Jewellery, coins and combs have been unearthed alongside the bodies.

THE HOSPITAL

There were three types of plague – bubonic, septicaemic and pneumonic – named depending on the part of the body affected. Bubonic plague victims had swollen lymph nodes, septicaemic had blood poisoning with dead and blackened tissue, and pneumonic had a bloody cough. The hospital was built in 1423, but with no treatment and little space, patients were piled three or four to a bed.

BELL TOWER

The plague was believed to be a divine punishment, so churches were erected so that prayers could be made for the sick. The bell tower also provided a convenient vantage point from which new arrivals could be monitored. This one was dedicated to Saint Mary of Nazareth, and the island became known as Nazaretum, or Lazzaretto, eventually giving rise to the word 'Lazaret', meaning isolation hospital.

SURVIVOR TRANSFER

Even though plague treatments were primitive, some people did manage to fight off the infection. Those souls who survived their ordeal on Lazzaretto Vecchio (the 'old' quarantine island) were sent to convalesce on Lazaretto Nuova (the 'new' island). Survivors travelled across the water, passing armed patrols and mixing with quarantined sailors and their cargo waiting to be allowed into Venice.

ARTIFICIAL ISLAND

The plague islands were located in the inland sea surrounding Venice, which is littered with submerged mudflats. When the tide went out, more land was revealed beneath the water and, as the demands on the island increased, this hidden space was reclaimed to accommodate more buildings, giving the island its distinctive artificial outline.

STAFF QUARTERS

Plague treatments were experimental and based on the best science of the day, which revolved around the idea that the body was filled with four humours — blood, phlegm, yellow bile and black bile — and that sickness resulted from them becoming imbalanced. The hospital's doctors would have attempted to rebalance their patients by bloodletting, and its body carriers would have been responsible for collecting and burying the dead.

SCOURGE

PLAGUE IS PUNISHMENT AND SUFFERING IS THE CURE
EUROPE, MID-14TH CENTURY

The act of self-mortification, or flagellation, had been common practice for holy men since the earliest decades of Christianity. As the Black Death ravaged Europe throughout the mid-14th century it erupted into a mass movement, powered by hysteria and the belief that this vile epidemic was a divine punishment.

The first outbreaks of public flagellation occurred in northern Italy in 1260, and the practice was soon carried to the rest of Europe, particularly central Europe and the Low Countries, where communities cowering under the shadow of pestilence adopted it as a desperate act of public contrition.

The most common tool of cleansing was the scourge, a whip with three tails that was often knotted or barbed with iron to inflict maximum pain that was worn on the waist.

The flagellants, or penitents, would march in a line two-by-two from town to town, robed and hooded in red crosses. Those at the front of the procession carried crucifixes and banners aloft, and they sung hymns begging for forgiveness. Twice a day the flagellants would stop in a town square in front of the church, form a circle, strip to the waist, remove their shoes and flay themselves until they bled.

The Dominican friar Heinrich von Herford (1300-1370), recalled, "Using these whips they beat and whipped their bare skin until their bodies were bruised and swollen and blood rained down, spattering the walls nearby. I have seen, when they whipped themselves, how sometimes those bits of metal penetrated the skin so deeply that it took more than two attempts to pull them out."

Finally, they would pray. The routine would be repeated a third time in the evening.

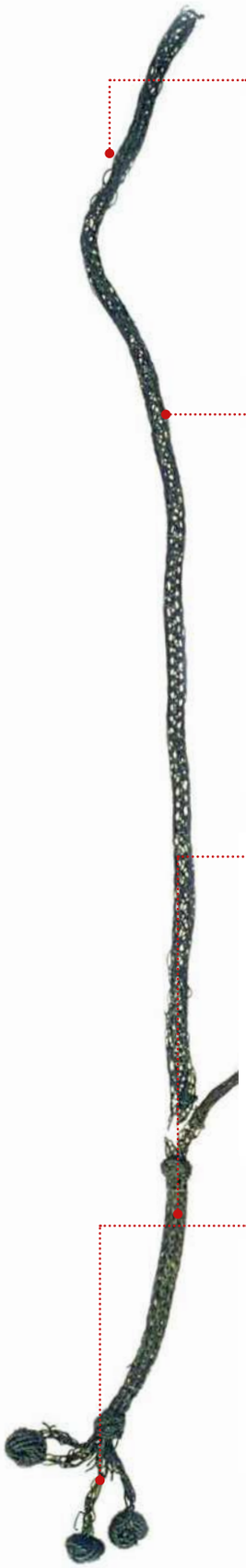
For townsfolk frustrated by the impotence of their priests and prayers, flagellation offered visceral answers, eye-catching spectacle and even supernatural healing.

The French-speaking chronicler Jean Froissart (1337-1405), who hailed from the Low Countries and penned several books, wrote of their audience that, "Some foolish women had cloths ready to catch the blood and smear it on their eyes, saying it was miraculous blood."

The practice soon peaked and quickly declined as papal bulls decried flagellation as heresy and secular authorities moved to restore public order following a series of grisly massacres of Jews by flagellants.

However the belief underpinning flagellation - that sickness was a punishment for sin - endured well into the Renaissance.

A 14th-century miniature shows a procession of flagellants whipping themselves with scourges as penance



CONSTANT COMPANION

Hung from the belt, the scourge was used at least three times a day for 33 and a half days (one day for each year of Christ's life) of suffering, with additional penance meted out for breaking the order's rules, such as talking out of turn or communicating with the opposite sex.

A SCOURGE FOR ALL

Though flagellants were penitent pilgrims, self-mortification was adopted by the faithful from across all social strata, and scourges could be as simple as knotted rope or as elaborate as leather whips with iron barbs. This one, found at Rievaulx Abbey in Yorkshire, is made from plaited copper alloy wire, which has ensured its survival against the ravages of time.

WHAT WOULD JESUS DO?

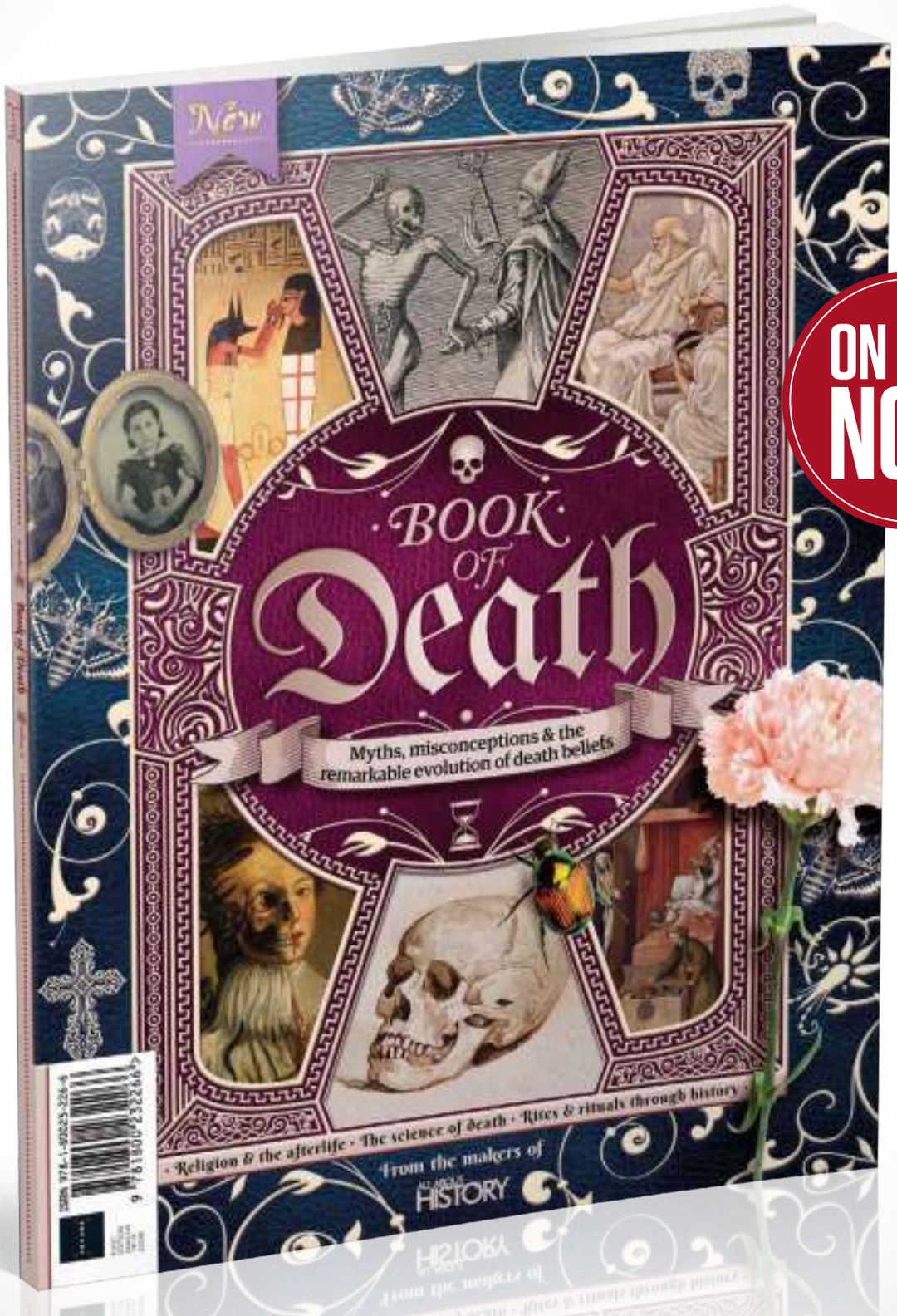
Flagellation as an act of penance has its roots in the Bible. Under Roman law those non-citizens condemned to crucifixion were scourged with whips barbed with small pieces of metal or bone, and in undergoing the experience the flagellants are following in Christ's footsteps.

STING IN THE TAIL

Knots or metal barbs tore at the flesh to create wicked, jagged wounds that repeated lashes would open further. These would then be washed in a mixture of wine and vinegar to help prevent infection.

MYTHS, MISCONCEPTIONS AND THE REMARKABLE EVOLUTION OF DEATH BELIEFS

Trace the extraordinary history of death, from the Ancient Egyptians to the American Civil War, and find out how science can help us to understand and demystify our fate.



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DARK ARTS OF THE PLAGUE DOCTORS

UNCOVER THE STRANGE CURES, PECULIAR POTIONS AND MACABRE APPEARANCE OF THE DOCTORS TASKED WITH BATTLING THE BLACK DEATH

WRITTEN BY **WINSTON BLACK**

You've seen him before: a mysterious figure, clad from head to toe in oiled Moroccan leather, wearing goggles and a beaked mask. He looks like a cross between a steampunk crow and the Grim Reaper. He's usually called a 'plague doctor', and a quick search online will turn up thousands of examples. Some of these images and costumes claim to represent genuine historical artefacts, while many others are new creations for Halloween and role playing. Thanks to the popularity of this costume, it has come to represent for modern audiences both the terrors of the Black Death and the foreignness of medieval medicine.

However, this sort of plague doctor did not appear until well after the Middle Ages, some three centuries after the Black Death first struck in the 1340s. There may have been a few doctors in the 17th and 18th centuries who wore this outfit, but most medieval and early modern physicians who studied and treated the plague did not. Nor was there a single class of physician in the later medieval and early modern periods who could be represented by a single outfit. Plague prevention and care came from university-trained physicians, surgeons, barbers, apothecaries, midwives, herbalists, priests, 'miracle workers' and a range of charlatans. Instead of relying on a single, special outfit, plague doctors instead employed a variety of therapeutic methods and environmental theories to protect themselves and their patients from the contagion of plague. Ideas about the cause and spread of the plague changed over the period of several centuries, as did the clothing worn by plague doctors and the methods they used to treat the disease. Even though these plague doctors, working long before the advent of germ theory and antibiotics, were unable to cure the plague, they deserve more credit than they usually receive for intelligently observing the spread and symptoms of plague and for giving people hope in an age of constant medical crisis.

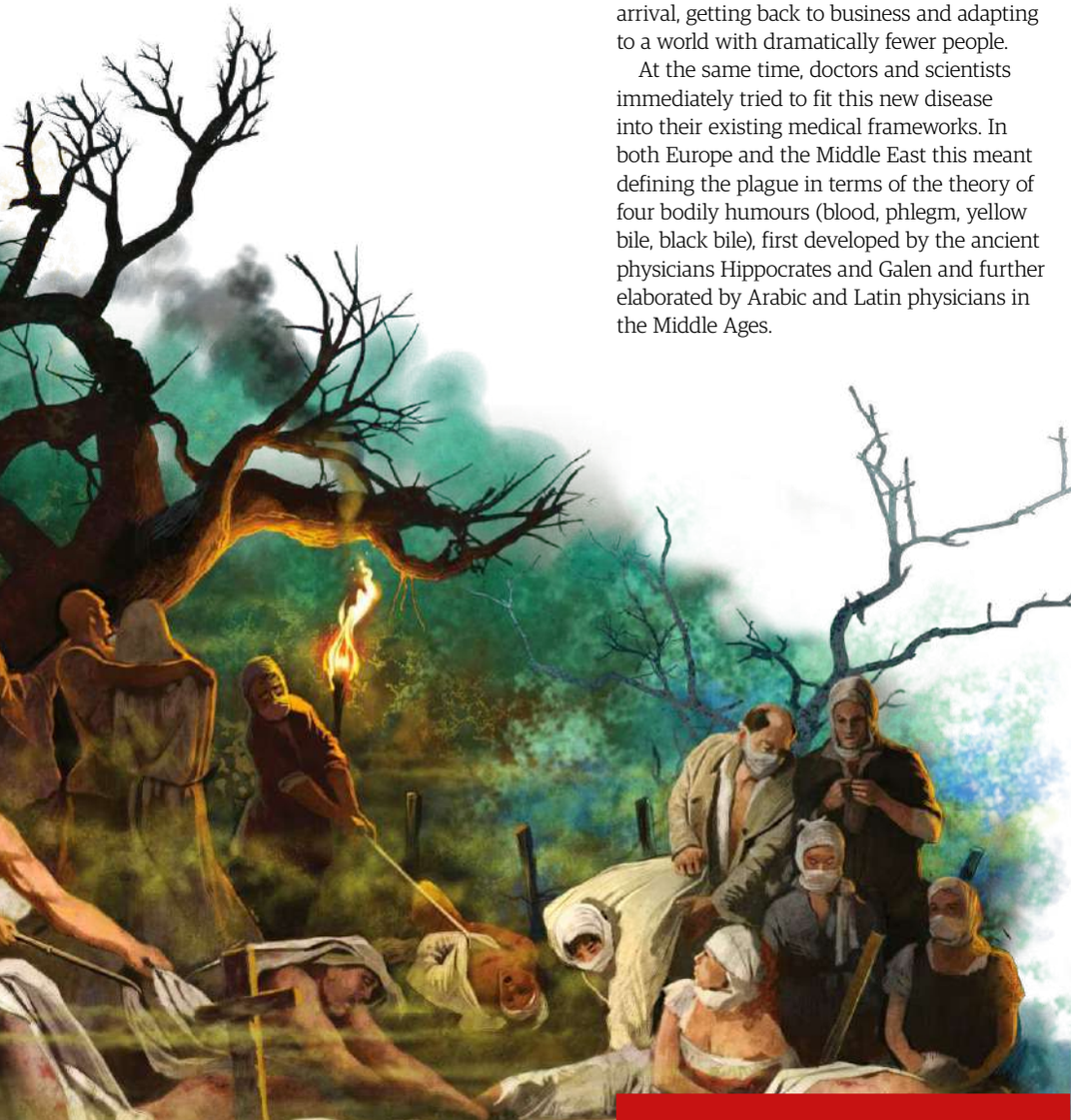
THE BLACK DEATH AND THE SECOND PLAGUE PANDEMIC

The Black Death of the 14th century is well known. When historians discuss 'the plague' they are usually referring to this epidemic of bubonic plague caused by the bacillus *Yersinia pestis*. The Black Death swept through the Middle East and Europe in the years 1346–1353 but it may have begun several decades earlier in the Qinghai Plateau of central Asia. Plague scholars estimate that 50-60 per cent of the population of Europe died during the Black Death, an even higher proportion than the often-cited 'one-third' of Europeans lost to the disease. Less well known is that the plague continued to strike Europe, the Middle East and beyond for the next four centuries, returning every ten to 20 years. This period of recurring plague epidemics between the 14th and 18th centuries is known as the Second Plague Pandemic. The so-called First Pandemic began in the 6th century CE and lasted until the 8th century CE, and the Third Pandemic lasted between 1860–1960. Few of the later outbreaks in the Second Plague Pandemic were as devastating as the Black Death, but they nonetheless continued to kill ten to 20 per cent of the population with each recurrence.

As shocking as it may seem to modern audiences, medieval and early modern people grew accustomed to the plague and took this periodic loss of population in their stride. Doctors and scientists worked to understand and treat plague better, especially in terms of preventing its arrival and spread in their communities. Many important developments in the history of medicine and health occurred against this backdrop of plague: the rebirth of

dissection, the discovery of the circulation of blood, and the development of public health measures among them. It is unclear why the Second Pandemic ended in Western Europe while it continued to strike in Russia and the Ottoman Empire well into the 19th century.

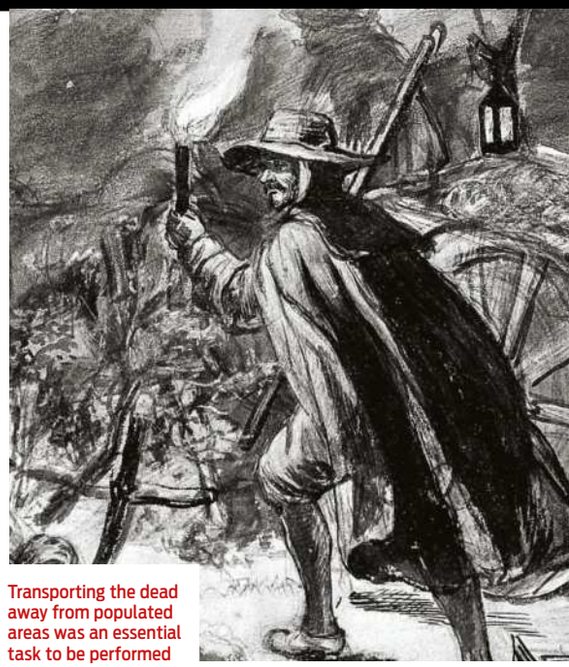
The Great Plague of London in 1665 was the last major outbreak in England, and plague likewise seems to have disappeared from Spanish and Germanic lands after the 17th century. The Plague of Marseilles, France, in 1720–1721 is considered to be the last major plague outbreak in Western Europe. Some historians argue that public health had improved to such an extent as to halt the spread of plague, especially through the systematic and effective use of sanitary legislation. Others point to evolutionary changes in human populations, rodent populations, or in the bacteria itself, but none of these claims seem to be holding up to recent discoveries in plague genetics. What is clear is that in the four centuries between the Black Death and the disappearance of plague from Europe, doctors worked tirelessly to explain, contain and treat this terrifying disease.



TREATING THE PLAGUE: BLOOD AND AIR

It's easy to imagine that medieval society completely collapsed in the face of a disease that quickly killed off over half the European population. This is the picture left by Giovanni Boccaccio, in the often-reproduced preface to his collection of stories known as *The Decameron*, written in the wake of the Black Death in around 1350. He describes the total failure of all the social, religious and educational networks in his community, which many people have taken to be true of all medieval society. But we must remember that Boccaccio was writing a work of fiction and describing events of only one plague outbreak in his native city of Florence. Archaeology and written records suggest that a few villages were indeed wiped out, but medieval historians have demonstrated that most communities rebounded within a year of the Black Death's arrival, getting back to business and adapting to a world with dramatically fewer people.

At the same time, doctors and scientists immediately tried to fit this new disease into their existing medical frameworks. In both Europe and the Middle East this meant defining the plague in terms of the theory of four bodily humours (blood, phlegm, yellow bile, black bile), first developed by the ancient physicians Hippocrates and Galen and further elaborated by Arabic and Latin physicians in the Middle Ages.



Transporting the dead away from populated areas was an essential task to be performed

Using these ancient and medieval medical theories, plague doctors argued that the Black Death was a pestilential fever that corrupted the humours, causing the horrific plague buboes, swollen with blood and pus. They recognised that buboes tended to form in the groin, armpits and neck, and explained them as the body expelling humours from the nearest major organs: the liver, heart, and brain, respectively.

According to these doctors, plague could be prevented by strengthening the humours or keeping them in balance through a detailed medical plan, or regimen, including changes in diet, drugs that caused beneficial vomiting and urination, and prophylactic bloodletting. All of these procedures were intended to remove corrupted humours from the body and to keep black bile (melancholia), which was usually considered the most dangerous of the humours, from dominating the body. If a patient did catch the plague, some doctors cautiously recommended lancing the bubo, as seen in a 15th-century image from a book on the plague by Hans Folz, a German barber surgeon.

Ancient and medieval medical authorities, following the legacy of Hippocrates, also recommended paying close attention to the qualities of the air when explaining epidemic diseases. They didn't need microscopes and laboratories to observe that some diseases seemed to come from within a person while others seemed to spread between people through the air. Plague was clearly contagious, striking entire communities at once, and it thus had to come from outside. Most doctors agreed that this external plague had to come from a corruption of the air itself, a corruption that was eventually known as miasma in the early modern period. Where the plague doctors disagreed was over the original source of miasma. Was it a universal

WHAT ABOUT 'RING AROUND THE ROSIE'?

THE FAMOUS NURSERY RHYME IS NOT MEDIEVAL AND NOT ABOUT THE BLACK DEATH

One of the most common 'facts' that people today know about the Black Death is that medieval people described it in a coded song, 'Ring Around the Rosie' (or 'Ring A Ring O' Roses'). The title supposedly describes circular, reddish plague boils. The 'pocket full of posies' protected their bearer from the poisonous miasma, which was thought to carry plague. 'Ashes, ashes' is the burning of plague victims' corpses (or in another variant, 'A-tishoo! A-tishoo!' describes the sneezing of the sick) and 'we all fall down' describes the devastation of the disease.

The trouble with this common popular theory is that there is no evidence for this rhyme until the 19th century, and there is no mention of the claimed secret meaning behind the rhyme until as recently as the 1960s.

If we closely compare the rhyme to actual medieval reactions to the plague, none of the pieces fit. Medieval people were much clearer in their descriptions of the disease, they never called the symptoms red or rose-coloured, sneezing was not a symptom of the plague, and they rarely if ever cremated the corpses of the plague's victims.

The only plausible part of the claim is the 'pocket full of posies', because plague doctors did at times recommend holding and smelling flowers to prevent contracting plague. But the belief that the song describes medieval reactions to the plague persists because it fits in with popular ideas about the foolishness and backwardness of medieval people. This popular myth overshadows the complexity of medieval medicine and the contributions of medieval physicians, who provided complex theories for the spread of the plague.

Die Pest, by Arnold Böcklin, depicts Death riding through a medieval town on a winged creature

The Great Plague of Marseille was the last major outbreak of bubonic plague in Western Europe

corruption sent directly by God to punish humanity? Was it a poisonous exhalation of the Earth caused by earthquakes opening subterranean caverns? Was it caused by exposed corpses or overflowing swamps? All of these theories were offered to explain the source of the poisonous miasma.

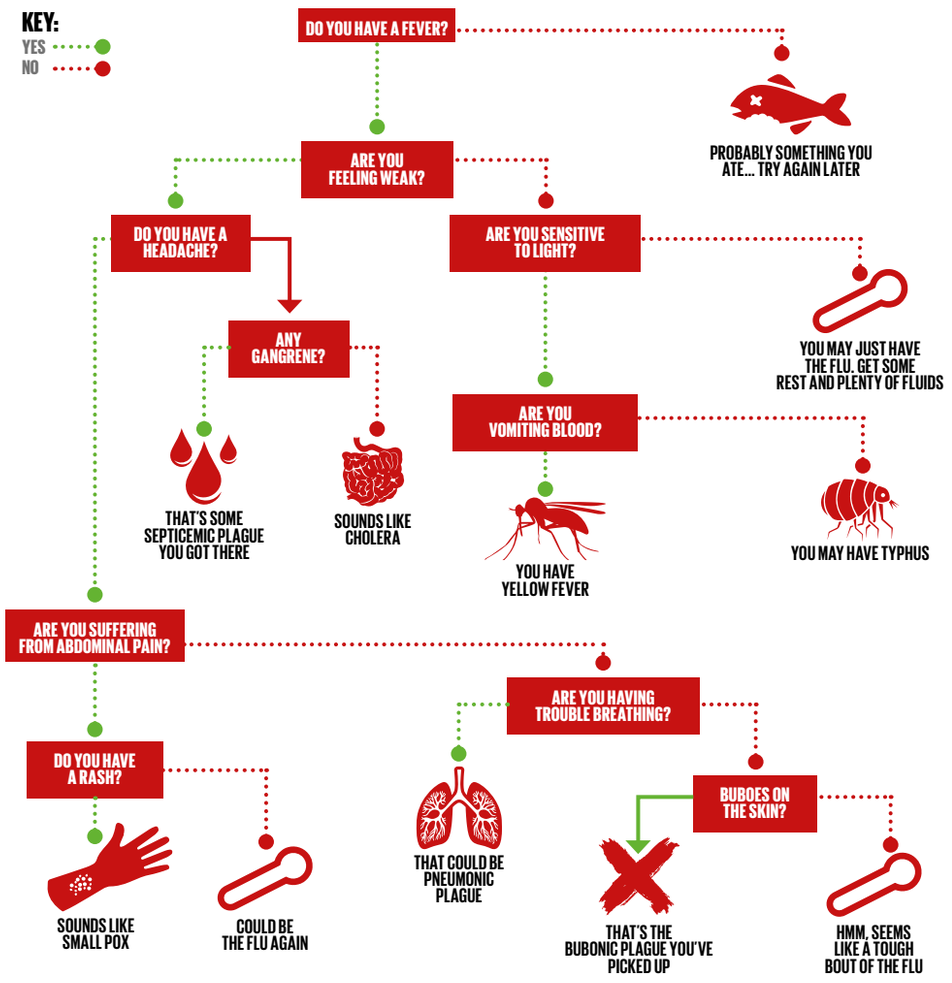
One of the most popular theories was described at length by the Faculty of Medicine at the University of Paris in a letter written to the king of France in 1348, who had asked the professors for their advice as the plague approached the royal capital. These learned authorities combined medicine with astrology, which was generally considered a serious science at that time, to explain the cause and spread of the plague: the air of the Earth, they said, was overheated and corrupted by a 1345 conjunction of the planets Mars, Saturn and Jupiter (all of which were considered hot, violent or corrupt in their astrological influence) in the zodiac sign of Aquarius (obviously a wet sign). This unnaturally hot and moist air blew across Asia towards Europe, causing plague wherever it passed. When medieval doctors referred to a 'pestilence', they often meant not the disease itself but the poisoned air that engendered the disease in human bodies.

To protect people from the pestilential air, doctors encouraged the wearing or holding of sweet or bitter substances, such as violets, wormwood, vinegar, or (if you were wealthy) a chunk of ambergris, a strongly scented secretion of a sperm whale's intestinal lining. They also recommended burning pitch, incense or bitter-smelling woods to purge and purify the air. And after the discovery and mastery of gunpowder in the later Middle Ages, they also recommended firing cannons to combat miasma with the gun smoke. In a woodcut from a 1491 medical textbook, *Fasciculus Medicinae*, we can see several of these preventive measures in action: the doctor holds a sponge, most likely soaked in vinegar, to his face, and his attendants hold long torches and an incense burner.

Many educated plague doctors wrote short books, known as plague treatises, to advise their peers and the literate public on plague prevention. They were already publishing these treatises during the Black Death itself. The Spanish physician Jacme d'Agramont wrote the

WHAT PLAGUE DO YOU HAVE?

ANSWER THESE QUESTIONS TO IDENTIFY YOUR AILMENT



During the Great Plague of London, infected households would have red crosses painted on their doors

first such work in April 1348. He composed it in his vernacular tongue of Catalan, rather than in the usual educated language of Latin, so that non-professionals could read it. Other early plague doctors include the Bolognese professor Gentile da Foligno, who died of the plague himself in 1348 after writing several casebooks on the subject, and Johannes von Göttingen, a German physician and bishop. It was not just European Christians who wrote about the plague though; the Muslim physicians Ibn Khātima and Ibn al-Khatib, both natives of the Islamicate caliphate of Granada, wrote treatises about the plague, as did the Jewish physician Abraham Caslari of Besalú. Groups of physicians in the faculties of medicine at the universities of Paris and Montpellier teamed up to write authoritative documents about the plague. Regardless of their religious or educational origins, almost all of these plague authors wrote about the same topics: how to identify the astrological and environmental signs of a coming plague; how to avoid the plague by keeping the humours in balance and cleaning one's home or city of potential sources of miasma; and how to treat the plague with herbal remedies, external plasters and bloodletting.

THE EVOLUTION OF PLAGUE MEDICINE

By the end of the Middle Ages, usually dated to about 1500, there were more doctors than ever and a greater variety of medical professionals who could focus on individual patients or epidemic diseases, urban and rural health issues, and local and foreign diseases. Historians of science and medicine also recognise a greater emphasis on detailed observation among early modern physicians, an essential feature of the developing Scientific Revolution. Doctors became increasingly adept at distinguishing and describing a wide range of swellings, blotches, fevers and other symptoms on the people in their communities,

PLAGUE DOCTOR BREAKDOWN

THE KEY ELEMENTS AND BACKGROUND OF THE FAMOUS 'MEDICO DELLA PESTE' COSTUME

AVIAN INFLUENCE

There is much debate over the origin of the bird-like mask of the plague doctor. In practical terms the beak was used as a kind of respirator, packed with herbs and oils like mint and lavender to block the bad smells, or miasma as it was known, from infecting the doctor. Symbolically, some suggest that it was inspired by the idea that birds spread the plague so looking like one might draw the sickness out of patients.

THE POMANDER

Since early plague doctors believed that the sickness was spread by miasma (corrupted air) they also thought that good, strong smells could ward it off. So it is that pomanders (an orange studded with cloves) held in a container with strong-scented liquids would be worn as a protection against illness and the general odours of the street. The simple form of the pomander is still used as a gift and symbol at Christmas and New Year.

NO EXPOSURE

The long overcoat with the mask tucked into the collar is an example of how the outfit was designed to reduce skin exposure to the air. The clothing is said to have been coated in suet (animal fat) as a barrier to stop the miasma penetrating the leather.

SYMBOLIC AND PRACTICAL

Many elements of the classic plague doctor costume play both practical and symbolic roles. The entire composition of the outfit is intended to prevent illness from spreading to the physician, but elements like the hat also helped to identify them as medical doctors.

KEEPING NOTES

Alongside attempting to treat plagues, the other very important function of the plague doctor was to record the spread of the disease and to bury and record the dead. As such, the doctors would have travelled with notebooks and kept extensive records of their patients that would prove useful to future studies.

MINIMAL CONTACT

The cane of the plague doctor was important in minimising even further the risks to the physician by preventing direct body-to-body contact with a plague patient. The cane could be used to interact with the body, lifting limbs and so forth as well as indicating areas for treatment to family members who were already exposed.

Charles Borromeo went into debt feeding the needy when Milan was hit by plague in 1576. He was later canonised

so they could determine whether an outbreak of disease was actually plague or another epidemic disease, such as typhus, influenza or dysentery.

This sort of medical observation was made possible through the growth of state-sponsored public health programmes aimed at preventing and curing disease throughout large populations. One of the best-known examples of later medieval public health is the establishment of quarantines (from the early modern Italian phrase, quaranta giorni, '40 days') to isolate populations and to keep potentially plague-ridden travellers and ships out of a city. Plague quarantines had been used at least since the 1370s in the wealthy city-states on the Mediterranean Sea, such as Florence, Mantua, Milan, Venice and Ragusa (modern-day Dubrovnik), but they were not widespread until the later 15th century.

For quarantine regulations to be effective, numerous cities and states necessarily had to work together, sending news of plague quickly and being honest about the presence and scope of an epidemic. Quarantine was made more effective through the establishment of permanent plague hospitals, or 'pesthouses'. These became a common feature of cities across Europe during the 16th and 17th centuries. Some were built within the city walls, but most were located well outside of a city to isolate confirmed and potential plague patients.

To help monitor and contain epidemic diseases and to run and staff the plague hospitals, first Italian city-states and then royal governments elsewhere in Europe established health boards and hired public physicians. One of the first such boards appeared in 1486, when the Republic of Venice founded a permanent Provveditori alla Sanità (Commission on Public Health) to oversee the rapid identification of plague, the deployment of trained physicians, the quarantine of the sick and the careful burial of the dead. Other cities responded much later. The city of Naples created a Magistrato della Sanità (Board of Health) in 1656 in reaction to a major outbreak of plague. The entire Kingdom of Naples also funded a royal Protomedicato, a medical tribunal that oversaw and licensed pharmacies and town physicians especially in times of plague.

The establishment of public health policy did not always work as planned: during the plagues of 1600 and 1625 in London, the College of Physicians refused to help the government fight the epidemic, as most of its members fled the city and urged everyone else to do so as well. However, during the Great Plague of 1665, some of the professional London physicians considered it their public duty to stay in the city and treat victims. They volunteered their services as official plague doctors.

THE MASKED PLAGUE DOCTOR

After nearly three centuries of treatments, treatises and policies for the plague we finally meet the beaked 'plague doctor', who too often represents the entire history of plague for popular audiences. The first mention of the costume that is so well known today is found in a work written in the mid-17th century by Charles de Lorme, a royal physician in the service of King Louis XIII of France. De Lorme wrote in his autobiography that earlier in his life, during a 1619 plague outbreak in Paris, he developed an outfit made entirely of Moroccan goat leather, including boots, breeches, a long coat, hat and gloves. The main feature of the costume is a tight-fitting mask, fitted with crystal eyepieces, extending into a beak about half a foot long filled with perfume or aromatic herbs. That beak is of course the most famous feature of the costume and was essential for a doctor to prevent the inhalation of pestilential miasma.

It is not clear if De Lorme deserves full credit for the invention of the plague doctor outfit, for there are signs of similar plague suits a little before his time. Physicians describing plagues in Grenoble in 1565 and Angers in 1582 mention the use of special hoods to prevent the transmission of pestilential air between the patient and the physician. There is no indication, however, that these costumes also included the long beak. In either case, it is surprising that it took between two and three centuries for physicians to design such an outfit, but it was during that time that physicians came to focus more on theories of interpersonal contagion than on a more universal miasma that could affect entire communities. Wearing these protective costumes suggests that doctors had grown more concerned about catching plague from a patient than from the air.

De Lorme left a written description of his plague costume, but our best visual evidence for the beaked plague doctor outfit comes only from the year 1656, when an especially devastating plague killed hundreds of thousands of people in Rome and Naples. At that time, several artists made engravings of the outfit worn by Italian plague doctors. Some of these artists took their subject seriously. For example, the German engraver Gerhart Altzenbach published a popular image of such a plague doctor, with text describing how his outfit protected the wearer against death. Even better known is Paulus Fürst's satirical engraving of a plague doctor, which he copied directly from Altzenbach. He called the image Doctor Schnabel von Rom, or 'Doctor Beaky from Rome', and describes how he does nothing but terrify people and take money from the dead and dying. It was Fürst who added some of the elements to the plague doctor that appear in versions of the outfit to this day,

FAMOUS PLAGUE PHYSICIANS

THE WRITERS WHOSE RECORDS HELPED TO CHRONICLE THE SPREAD OF EPIDEMICS

ABRAHAM CASLARI (ACTIVE 1323–1349)
A Jewish physician from Besalú, Spain, Caslari was the translator of Arabic and Latin medical treatises and the author of a plague treatise in Hebrew.

GENTILE DA FOLIGNO (D.1348).
Italian professor of medicine and author of multiple treatises on plague for different audiences. He apparently died while treating plague patients.

GUY DE CHAULIAC (CA.1300–1368),
French physician and surgeon who described the spread and treatment of plague in his book *Chirurgia Magna* (Great Surgery). He gained fame as the personal physician to Clement VI (1342–1352), the pope during the Black Death.

IBN KHĀTIMA (D.CA.1369) Muslim physician and poet in Spain. Wrote about his experience diagnosing and treating plague patients in Almería in the work *Description and Remedy For Escaping Plague* (1349).

IBN AL-KHATIB (D.1374) A Muslim author and physician in the kingdom of Granada in southern Iberia and friend of Ibn Khātima. He wrote *A Very Useful Inquiry Into the Horrible Sickness* in the period 1349–1352, in which he argued that plague was contagious, a concept that went against some interpretations of Islamic law.

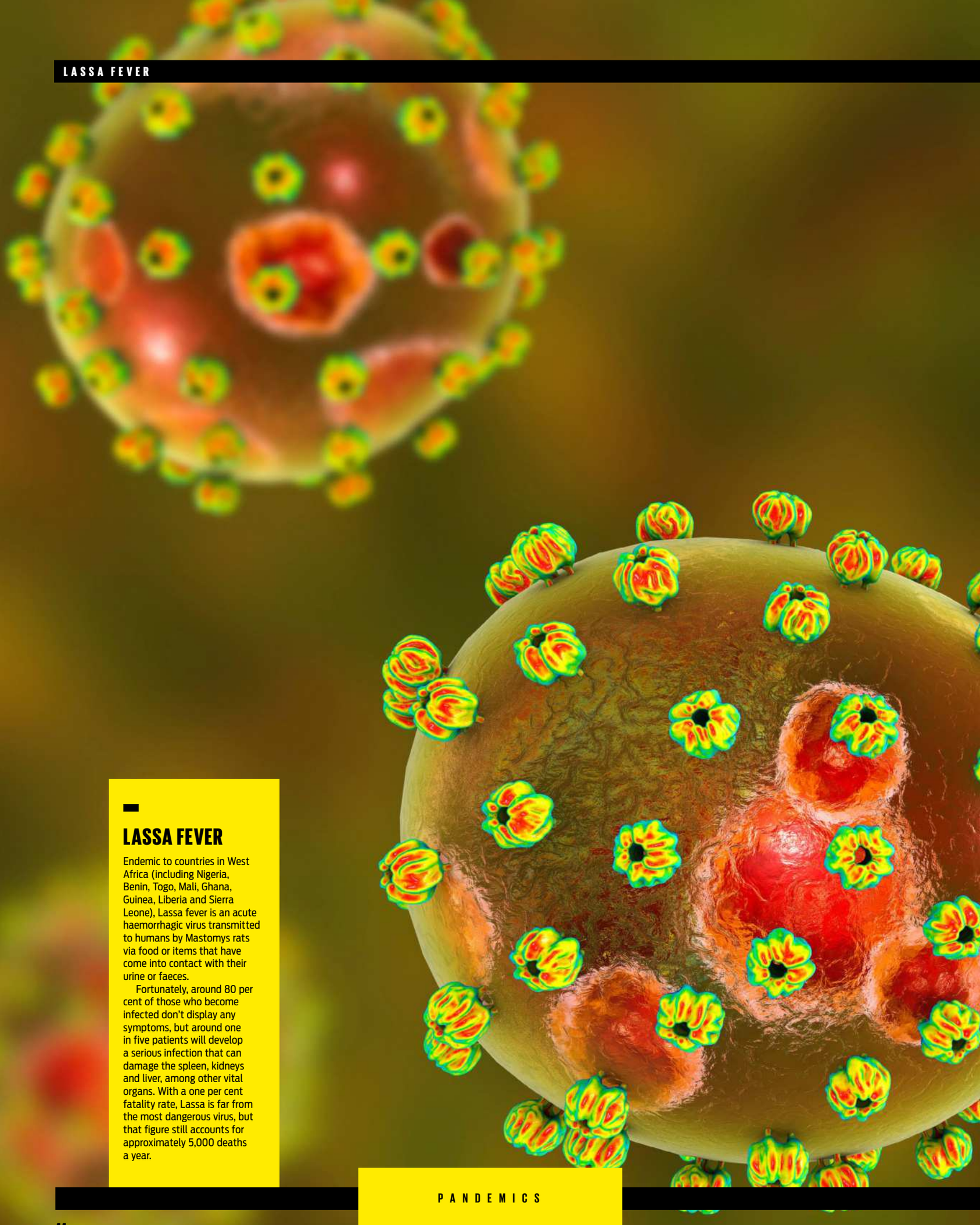
JACME D'AGRAMONT (D.1348). Professor of medicine at the University of Lérida. He wrote the earliest-dated medieval plague treatise, entitled *Regimen of Protection Against Epidemics.*

JEAN JACMÉ (ACTIVE CA.1364)
A personal physician to the king of France and the pope, as well as chancellor of the University of Montpellier. He wrote a short treatise on the plague that was copied and spread more widely by Bengt Knutsson, a 15th-century bishop in Sweden.

JOHN OF BURGUNDY (ACTIVE CA.1365)
Wrote one of the most popular plague treatises, which he directed to non-professional audiences. It was translated from Latin into many European vernaculars and copied and printed widely for more than 300 years.

such as the claw-like gloves and the pointing stick topped by a bat-winged hourglass. These elements belong to satire and not to historical reality, but they have nonetheless shaped much of how the stereotypical plague doctor is understood today.

The engravings of Altzenbach and Fürst may also have inspired the inclusion of the plague doctor, or Medico della Peste, as a standard character of the Italian commedia dell'arte since the 17th century. The plague doctor, and especially his beaked mask, has become one of the most popular costumes in the Carnevale, or Carnival of Venice. In fact, some costume historians have argued that the beaked plague doctor was nothing but a fictional and comedic character at first, and that he actually inspired genuine doctors to use the costume during the outbreaks of 1656 and 1720. Without more informative written reports and images from this period, which can help us understand better whether the outfit was actually used, it is impossible to tell which came first: the plague outfit or the Carnival costume. What we do know is that the beaked plague doctor represents three centuries of physicians, scientists and health officials thinking about the spread and prevention of plague. They represent changing ideas about the causes and transmission of disease, about the relationship between doctors and patients, and about the role of the state in protecting public health.



LASSA FEVER

Endemic to countries in West Africa (including Nigeria, Benin, Togo, Mali, Ghana, Guinea, Liberia and Sierra Leone), Lassa fever is an acute haemorrhagic virus transmitted to humans by Mastomys rats via food or items that have come into contact with their urine or faeces.

Fortunately, around 80 per cent of those who become infected don't display any symptoms, but around one in five patients will develop a serious infection that can damage the spleen, kidneys and liver, among other vital organs. With a one per cent fatality rate, Lassa is far from the most dangerous virus, but that figure still accounts for approximately 5,000 deaths a year.

HOW TO TREAT THE BLACK DEATH

FIGHT THE GREAT PESTILENCE JUST AS MEDIEVAL PHYSICIANS DID ENGLAND

When the Black Death came to England in 1348, it left a trail of devastation in its wake. More than 1 million people fell victim to the disease that had already swept through Europe, wiping out millions as it continued its merciless progress through the land.

The cause of the Great Pestilence was a mystery, and, as doctors struggled to find a cure, some outlandish methods of healing the infection emerged. In this simple guide, you'll learn how to treat a case of the Black Death just as doctors in the Middle Ages did. Whether you'll live to tell the tale is another story.

THE DOCTOR IS IN
Plague doctors might look fearsome, but they were actually helpless against the scourge of the Great Pestilence.

MEET THE PATIENT
Stricken with pain, the patient suffering from the Black Death faces a bleak and uncertain future.

CUT THEM OPEN
Using a sharp blade, open the vein of the inner elbow on the side where the patient is experiencing the most pain.

APPLY THE LEECHES
Apply leeches to the wound. If the infection is already severe, open more veins and apply more leeches.

REMOVE THE LEECHES
Once the leeches have grown fat and fallen off, return them to their jar and dress the wound.

WHAT YOU'LL NEED...

"THE CAUSE OF THE GREAT PESTILENCE WAS A MYSTERY, AND, AS DOCTORS STRUGGLED TO FIND A CURE, SOME OUTLANDISH METHODS OF HEALING THE INFECTION EMERGED"

01 TIME TO BLEED

As soon as the patient shows even the slightest symptoms of the plague, there's no time to lose. Ask him which side of his body is the most painful and have the surgeon open a vein in the arm on that side or, even better, apply leeches liberally to the painful areas. Bleed him until his soreness dissipates.

02 TAKE YOUR MEDICINE

There are all sorts of natural remedies, known as plague waters, available for the Black Death, and your local doctor will know which one is right for your patient. To make your own, mix angelica, juniper, figs, saffron and vinegar. Add a little nutmeg to taste and serve hot. This will encourage the patient to sweat out the pestilence.

HOW NOT TO DISPOSE OF A BODY

As the Black Death ravaged the lands, plague pits became a familiar sight, along with vast bonfires on which the bodies of the dead were burned. In the Crimean city of Caffa in 1347, however, the Mongolian Tatars decided on a very novel way of disposing of their plague dead.

Tatar warriors had besieged the Italian inhabitants of Caffa without success for months, failing in their bid to drive its people from the city. Now, with their ranks depleted by plague, the dispirited Tatars began catapulting plague-ridden corpses over the city walls. The Italian populace took fright and many fled Caffa for their homeland, bringing the Black Death with them to mainland Europe.

This incident is one of the earliest known examples of biological warfare. Though the impact on the mainland was devastating, the Tatars did not conquer Caffa and the city remained under Italian control.

03 BURST BUBOES

As the plague progresses, the telltale buboes will start to appear, most commonly in the groin and armpit. These must be purged without delay as they contain the disease. Apply a hot poultice of lily root, ale grounds and mallow to bring out the boil, then pierce the bottom of the buboes to drain out the poison.

04 SWEAT IT OUT

If your patient is mobile, encourage him to sit between two fires; if he is in bed, surround him with bottles filled with hot water. The patient should sweat for a minimum of three hours, preferably even more, as this will encourage the infection out of the body. Dry him off, dress him warmly and put him back to bed.

05 FUMIGATE THE 'BAD AIR'

While the patient rests, it's time to fumigate the miasma. Cleansing the air will help ward off the plague and treat those already suffering. Hang posies of rosemary, sage and lavender in the house, particularly in the sickroom. You can increase the efficacy by keeping a heated bowl of vinegar near the patient and allowing the steam to disinfect the air.

06 REPEAT AD NAUSEAM

Repeat the treatments, occasionally feeding the patient small amounts of simple food such as chicken or veal washed down with mild ales. The patient will soon be on the road to recovery or, sadly, taking a turn for the worst. If your efforts aren't successful, don't feel too disappointed — millions have already fallen victim to the Black Death.

IF THAT DOESN'T WORK, THEN TRY THESE CURES...

FLAGELLATE

Join a flagellation procession and whip yourself for your sins, thus earning God's forgiveness and ridding yourself of plague.

CHICKENS

Pluck a live chicken and hold it against your buboes. This will draw the poison out of you and into the unsuspecting bird.

PIGEONS

If chickens don't work, slice up a dead pigeon and rub its entrails all over your body.

FAECES

Open the buboes and smear them with a paste made from human faeces, tree resin and plant roots. Be sure to bind the wounds up tight!

EMERALDS

Richer patients can crush emeralds into powder, mix them with broth and down them in one gulp.

INSIDE AN APOTHECARY

WESTERN EUROPE, 1100

An apothecary was a busy place in medieval times since it was where substances used in medicine were sold to patients, physicians and surgeons. Apothecaries were, to a great extent, the predecessor to modern pharmacists, mixing the smallest of quantities of herbs and spices to create treatments while offering medical advice and carrying out a small range of services.

It could be imagined to be a place of wonder and hope, with shelves packed full of jars and vials filled with powders and liquids. The air would be filled with the scent of exotic spices, and some apothecaries would work hard to maintain a feeling of mystique.

They wanted people to feel both amazed and reassured that the sometimes off-beat ingredients (fat, flayed cats, hedgehog grease, bear fat and virgin wax were involved in treatments for throat infections) would do them great good and encourage a purchase.

The shops could be found across Europe, where streets were often named after them, especially when a handful existed side by side (Apothecary Street in London is one such case). For those who worked in them, there was much pressure, particularly as demands for cures grew and greater quantities of ingredients became necessary. Apothecaries could be blamed if a patient's condition did not improve, but they were seldom thanked if it did.

It didn't seem to matter that apothecaries did not have any formal training to begin with (examinations were introduced in the 15th century). Indeed, there were many cases where apothecaries would have dual roles, perhaps doubling as a barber or even performing surgery.

It was not unusual for medicine to be done 'on the side', either, since the shops would sell perfumes, items for food, wines for general consumption and even stationary. Neither, come to that, was it rare for apothecaries to give advice or even diagnose illness even though the law stated their role was purely to supply medicine. Few found themselves prosecuted.

SELF-RELIANCE

Initially, apothecaries would cultivate their own plants and herbs in a garden plot outside. This would help them to cut down on costs and ensure that there was enough of a supply to produce the necessary treatments. As time went on and demand rose they would purchase their ingredients from a growing number of suppliers.

TRADING IN BEAUTY

As well as helping people back to health, an apothecary would make and sell perfume and other beauty products in much the same way as a modern-day pharmacy. Often ingredients would have a dual use. Tragacanth, a natural gum taken from the dried sap of Middle Eastern legumes, for example, was used in both a perfume and cough medicine.

LIVE ANIMALS

Typically, an apothecary would also have live animals at his disposal, although perhaps not always permanently on the premises (to aid gout, for instance, an owl was plucked clean, opened, salted, cooked and pounded with boar's grease). Medieval cures for burns involved rubbing the slime of live snails on a wound. Bizarre at is sounds, this did have some scientific grounding: the slime has anti-inflammatory, antioxidant and antibiotic properties.

TREATING PATIENTS

Although much of an apothecary's work was selling raw ingredients and creating medicines to a recipe written in Latin, they would also be called upon to diagnose illness and prescribe treatments to help cure or relieve an illness. It would appear the training, however, was not formal but passed down in an apprentice-like scheme over many years, and it could involve tongue scraping, tooth extraction and the use of knives (treated with sterilisation equipment, of course).

RAW INGREDIENTS

Behind the counter, in jars on the shelves lining the walls, was an assortment of herbs and spices used in the preparation of the medicines. There would be pepper, ginger, saffron, nutmeg and cloves, cumin, aniseed, rosemary, fennel and nuts, among many other ingredients. Curing migraines, for example, entailed boiling barley, betony, vervain and other herbs before wrapping them in a cloth and applying to the patient's brow. In this case, the apothecaries were not far off the mark – betony and vervain can be found in modern treatments.

DIFFERENT LIQUIDS

Wines, cordials and syrups would also be contained within many of the jars. Wine was thought to be useful in attaining healthy blood, with the finest, aromatic and pleasant-tasting tipples of the most benefit. It would be boiled to allow other ingredients to dissolve or it would be drunk 'neat' – the idea being that it could enter the blood stream directly and generate blood. To that end, wine was believed to aid the absorption of other medicines.

MORTAR AND PESTLE

The best way to crush and grind herbs, spices and other ingredients was with a mortar and pestle. Apothecaries would have a number of them in various shapes and sizes, the smaller ones being particularly good for the grinding of fine powders, whether wet or dry, and larger ones for bulkier ingredients.

WEIGHTS AND SCALES

In most cases, only tiny amounts of each ingredient were used, and it was important to get the balance right. For that reason, the weights and scales of an apothecary were invaluable, and they used the Troy method based on the weight of a grain of wheat: a Troy ounce was 480 grains or 31.1 grams and a Troy pound 5,760 grains.

PREPARATION AREA

Apothecaries would generally prepare the medicines using their ingredients out of sight of the purchaser, working to age-old recipes that they would refuse to divulge. They worried about potentially giving a rival an advantage by revealing their secrets, so they would work diligently in a back room and hope their cures or treatment would work so that word would spread about their personal effectiveness.

PUBLIC-FACING

Many apothecaries ran their own small shops such as the one pictured here, serving medicine to members of the public from behind a counter in the front section of dedicated retail premises. Visiting patients would trust the men to diagnose their conditions and they would buy products deemed capable of curing or relieving their ills. Sometimes an apothecary shop was based in the apothecary's home.

THE ANATOMY OF A PHYSICIAN

WESTERN EUROPE, 1215

JAR OF URINE

Patients would be asked to provide a urine sample, and this formed a fundamental part of a physician's diagnosis (together with an examination of blood and stools). They would compare the colour of the urine with a chart in a medical treatise, holding the flask up to the light for a good look. Diagnoses would be looked up in a vade mecum book.

EDUCATED MEN

High-end physicians in the Middle Ages were university educated and their medicine was rooted in the writings of ancient Greeks such as Hippocrates and early medieval Arab physicians. They treated aristocrats and royalty, explaining illness as an imbalance of the four humours (or distinct bodily fluids): black bile, yellow bile, phlegm and blood.

A CRUCIFIX

Physicians saw no distinction between medicine and faith, and disease could also be attributed to everything from demons and sin to the stars and punishment from God. Although they were recognised as a distinct professional class in 1215, their treatments – be they bloodletting or herbal remedies – went hand-in-hand with prayer and relics. To the medieval worldview, all things in life possessed a spiritual dimension.

A BUNCH OF POSIES

It was widely thought that diseases were carried by smell, so physicians would seek to protect themselves by masking any stench. Posies were a popular choice, but oranges were also used. Flowers also came in handy for treating smallpox – as well as giving patients red food and drinks and wrapping them in red cloths, physicians would ground red roses with bamboo juice.

MONEY PURSE

Physicians would always charge high fees for their services, with renowned practitioners in England typically commanding 100 marks for their treatments (a mark being a medieval unit of account worth 160 pence). This would be the equivalent of some £48,000 today, with many physicians put on a retainer fee that attached them to a royal or noble household.

CUTTING TREATMENTS

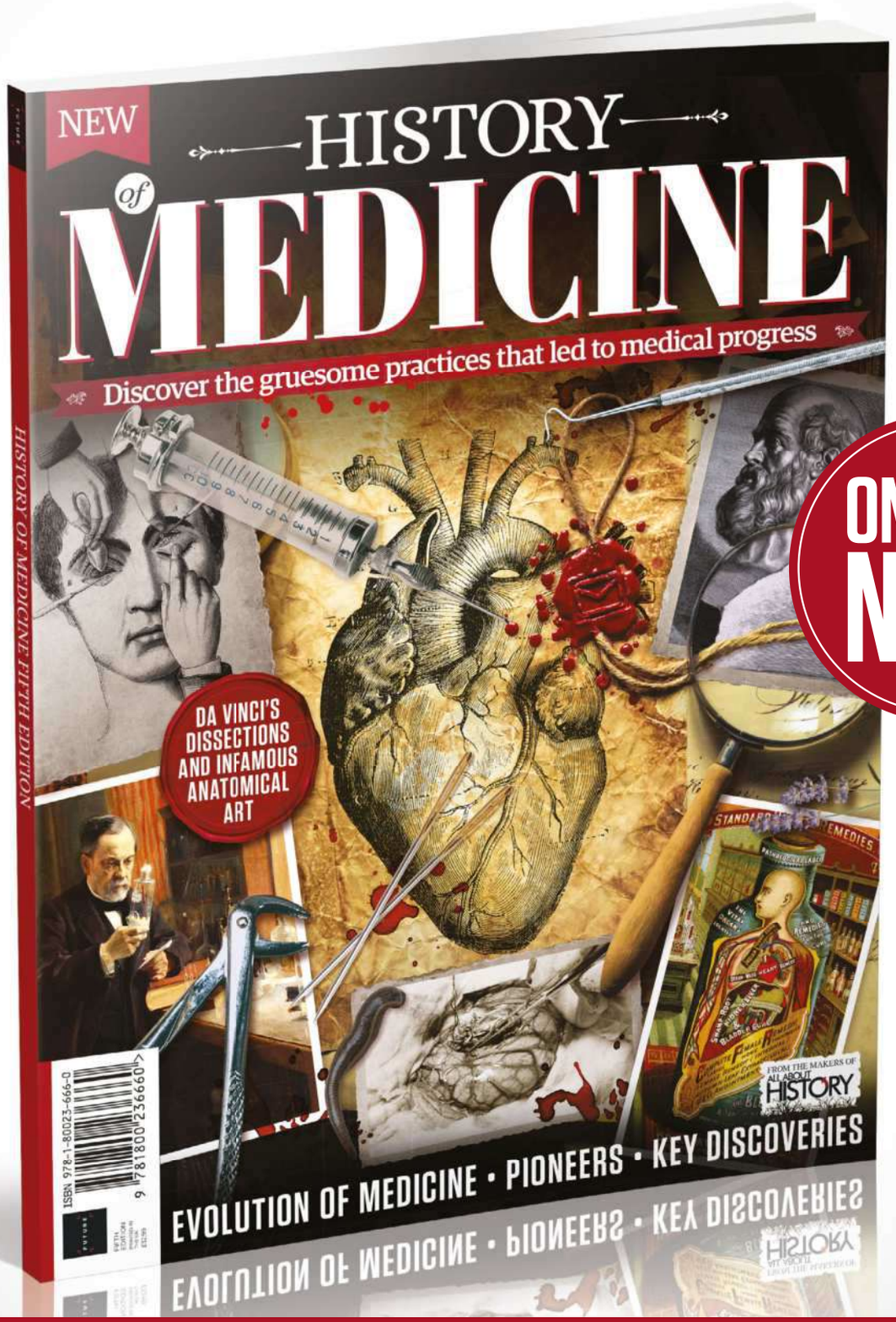
There were some extreme cures for disease. Inflamed lymph nodes within the armpit or groin areas would be sliced open to allow the pus to drain, while trepanation would see a hole drilled into the patient's skull so that blood build-up could be relieved or intracranial diseases cured. Being made to vomit – another way of balancing the body – seemed tame in comparison.

DRAWING OF BLOOD

Working on the basis that fire, water, earth and air controlled the humours, physicians believed the body would be 'balanced' by removing 'bad blood' (they thought blood was static and stagnated in certain parts of the body). Ailments were therefore treated by clamping leeches to the patient's skin (sometimes to the eyes). Over time, physicians themselves were nicknamed leeches.

DISCOVER THE ORIGINS AND EVOLUTION OF MEDICINE

This special edition charts the landmark medical discoveries and treatments through history, from gruesome primitive practices like trepanning up to the miraculous life-saving technologies available today.



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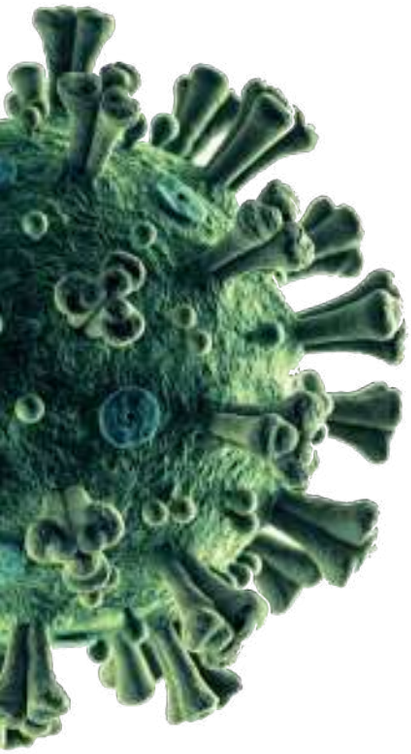
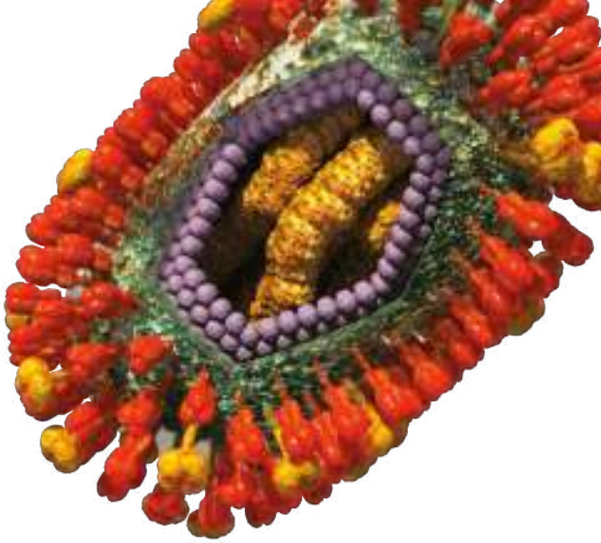
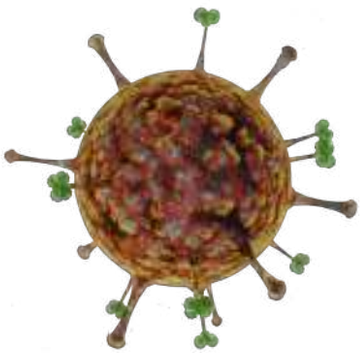
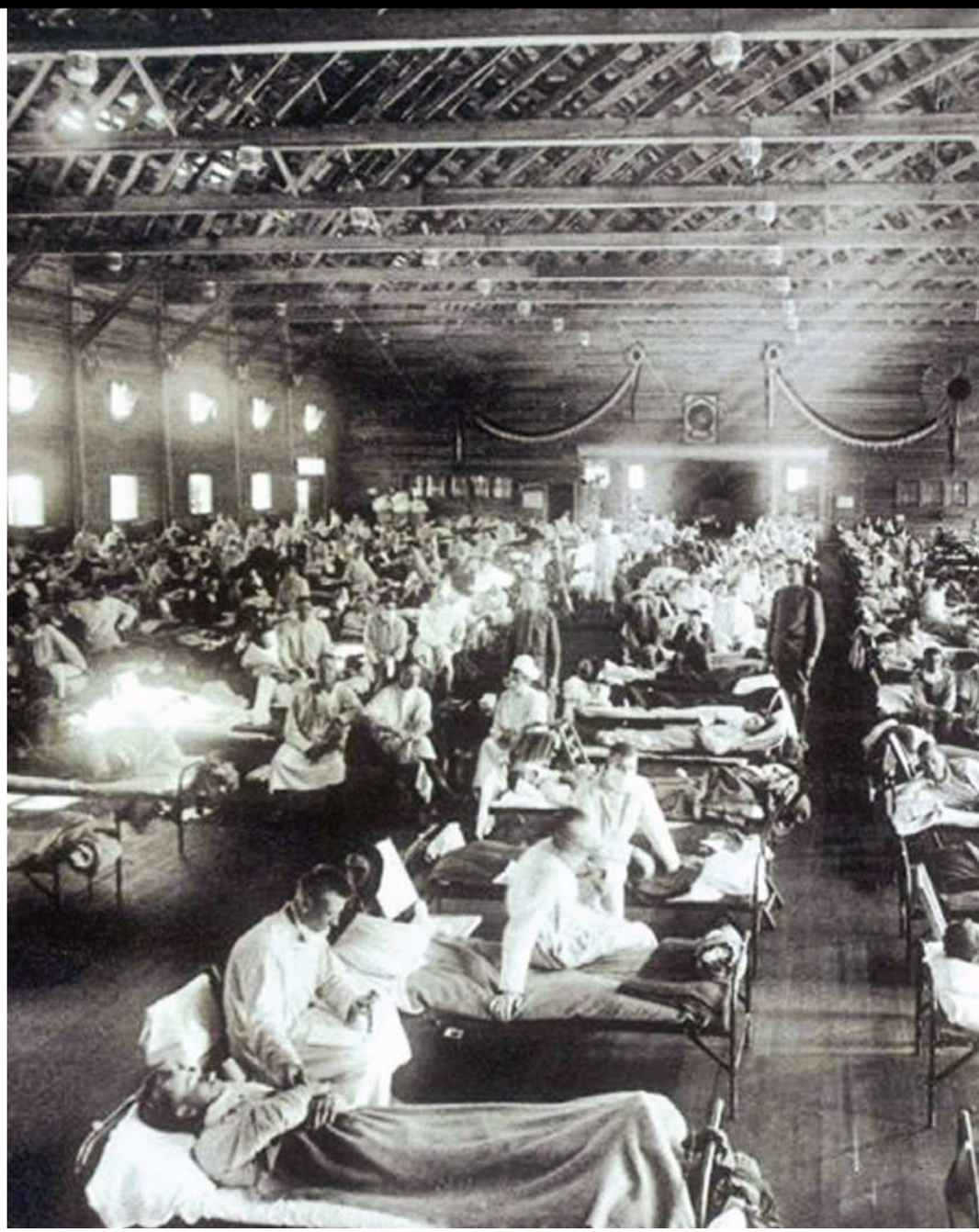




INFLUE



NZA



SPANISH FLU

THE CONTAGION OF 1918 CLAIMED THE LIVES OF MORE PEOPLE THAN THE WHOLE OF WORLD WAR I. UNCOVER THE ORIGINS AND AFTERMATH OF THIS MODERN BLACK DEATH

WRITTEN BY **NELL DARBY**

A group of children play in one of London's parks. They are happy and giggling, pleased that the council has closed their school for the week. The streets they walked through to get to this park were quieter than usual, and when they passed adults, they had scarves clutched to their mouths and noses. Some even wore odd-looking masks, like the injured soldiers have been wearing since they returned from the war to keep people from staring at the burns and the scars they now bear. The children start singing, and even though many adults near them are closeted in their houses and flats, their windows clamped shut, they can still hear the high-pitched words of the children:

I had a little bird
Its name was Enza
I opened the window
And in-flew-Enza

The song's words conceal the true horror behind this seemingly cheerful picture. A strain of influenza – known as Spanish flu – has struck not only the local community but the wider world, spreading rapidly and striking indiscriminately. The young, the old, the sick and the healthy are being infected, and at least ten per cent of everyone contaminated will die. This is a world that has just endured the horrors of war. Many families will not see their fathers, brothers or husbands return from the battlefields, and others will see them come home as changed men, damaged by their experiences. Still, there's hope everything will go back to what it was, but it quickly becomes clear there is a new, even deadlier battle on the horizon.

The Great War might even have been responsible for the Spanish flu pandemic, which ended up killing millions of people worldwide. Towards the end of the war, many soldiers, in their cramped, dirty and damp trenches in northern France, were falling sick. Their tendency to become ill was put down to 'world-weariness' caused by their experiences – their immune systems were weakened and they were malnourished, meaning their bodies weren't strong enough to fight off infection. They couldn't eat, they had sore throats and started to suffer with headaches.

Their illnesses, which were known locally as 'la grippe', were contagious and spread among the soldiers. Within around three days, most soldiers would usually start to feel better – but not all, and some wouldn't make it home. Lieutenant Leo Mansfield Matthews, aged 35, had volunteered for active service, and had been on the front since September 1916. He died in hospital there on 25 June 1918, remembered by his fellow soldiers as a bright, confident man who managed to cheer up his men "even in the most depressing moments".

During the summer of 1918, troops started to return to Britain, travelling by train. They brought with them the underlying virus

Farmers attempting to protect themselves from the Spanish flu in Canada, 1918

that had made them ill, spreading it out across cities, towns and villages. For some of their families, the happiness they felt would soon be replaced by horror and grief. There was no rapid recovery for either soldiers or civilians. The virus particularly hit the young, those aged between 20 and 30. The *Times* reported "Persons who feel perfectly well and are able to go about their business at 10 o'clock in the morning [are] prostrate at noon."

From the initial symptoms of a sore head and fatigue, suffers would develop a dry, hacking cough, a loss of appetite, stomach problems, and then, on the second day, excessive sweating. The respiratory organs might start to become affected, increasing the risk of pneumonia. This happened with Howard Brooks, a 19-year-old Londoner who caught influenza and died of pneumonia. It also happened with 27-year-old naval instructor George Carter, who died of septic pneumonia following influenza. There were no antibiotics – no medicine that could make them feel better. Instead, the advice amounted to fresh air, cleanliness, a good diet and 'constant disinfection'.

HITTING THE HEADLINES

The papers, from January 1918 onwards, were reporting cases of influenza without making any link between them explicit. Instead, the instances were reported as isolated, unrelated cases. People were dying in the UK of influenza, but it was Spain – one of the earliest countries to be hit and which gave its name to this

SYMPTOMS OF THE KILLER FLU

THE DEADLY DISEASE COULD SEEM HARMLESS AT FIRST

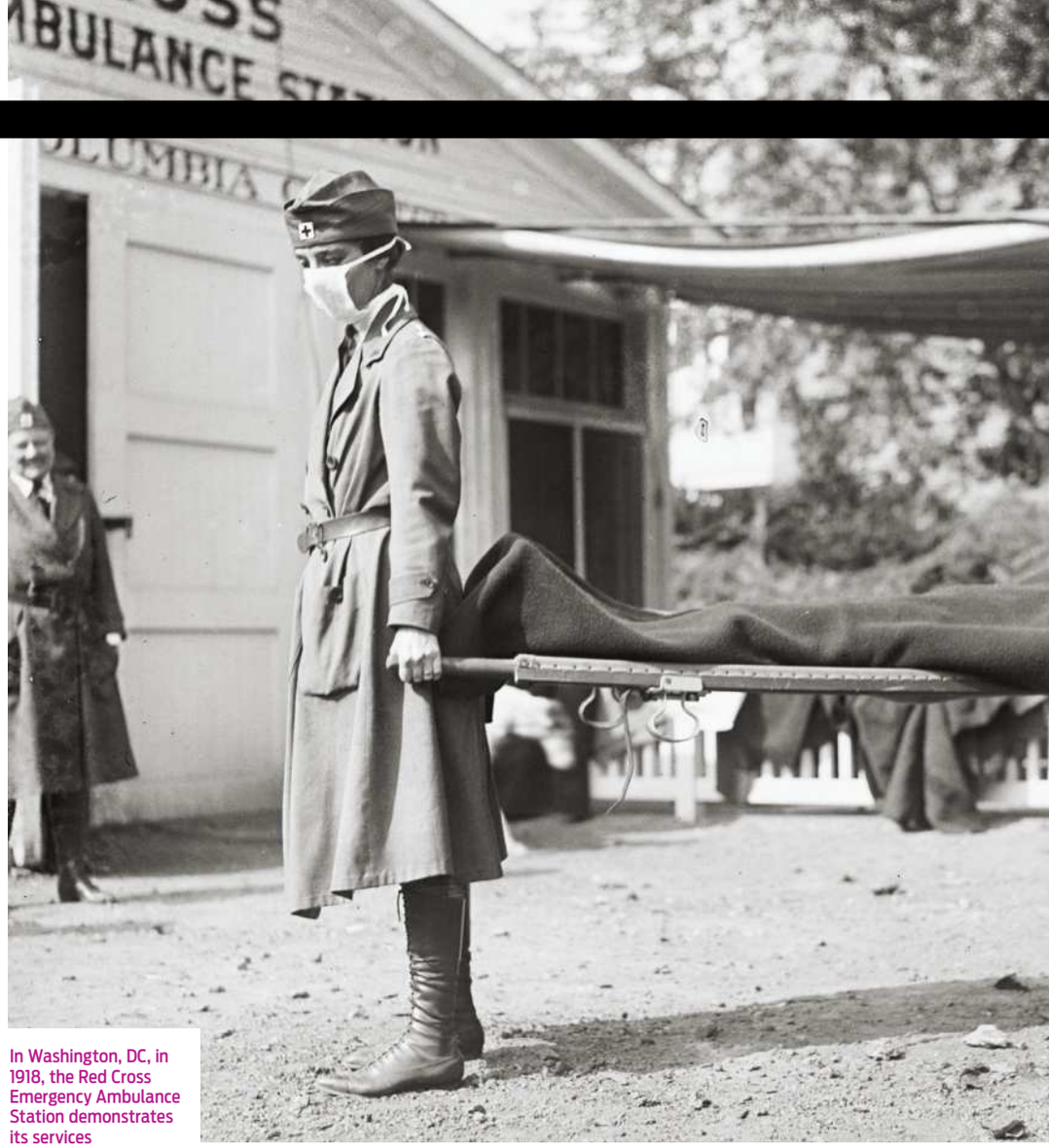
- ☑ FEVER
- ☑ NAUSEA
- ☑ ACHING LIMBS
- ☑ COUGHING
- ☑ BLOODSHOT EYES
- ☑ HEADACHES
- ☑ NOSEBLEEDS
- ☑ VOMITING
- ☑ DIARRHOEA

strain of the virus – that received the most attention. However, even in May 1918, the Spanish ambassador in London had stated, "The epidemic which has broken out in Spain is not of a serious character. The illness presents the symptoms of influenza with slight gastric disturbance." But a week later, the *Times*, which had reported the ambassador's PR attempt as a true statement, was taking a different, more panicked approach.

By now, 700 people had died in ten days in Spain, and it was being reported that more than 100,000 people there had become infected within the two weeks since it had "appeared in Madrid". The papers now regretted their previous flippant tone and stated that the epidemic had "passed the joking stage". The flu had begun to spread beyond Spain and reached Morocco. The King of Spain, Alfonso XIII, had been struck down with it, along with leading politicians. Where people worked or lived in close confines to each other, such as in schools, barracks and government buildings, 30 to 40 per cent of their populations were becoming infected. The Madrid tram system had to be reduced, and the telegraph service was disturbed – in both cases because there were not enough healthy employees available to work. Pressure was being put on the medical service and supplies, and they were failing.

Soon it was being reported that the Spanish flu had spread to other countries in mainland Europe. One high-profile victim was the sultan of Turkey, whose death was reported in the *Daily Mirror* on 5 July 1918, the paper regarding his passing as rather trivial as, "...he was regarded as a nonentity in the hands of his advisers". Vienna and Budapest were suffering; parts of Germany and France were similarly affected. Many children in Berlin schools were reported as being ill and off school, and in the armament and munitions works absences were affecting production. In Frankfurt's factories, up to 50 per cent of workers were ill. The epidemic then reached Switzerland, with 7,000 cases being reported among soldiers of the Swiss army, and half of the population of Môtiers in the Vale-de-Travers were sick with the flu.

Initially, when the epidemic was still seen as being restricted to Spain, it was noted that men were more likely to be infected than women and that adults were at far more risk than children. Similarly, once it became a pandemic and had



In Washington, DC, in 1918, the Red Cross Emergency Ambulance Station demonstrates its services

Harold Lockwood, one of the most famous film stars of the 1910s, was one of the victims of Spanish flu

spread to Switzerland, it was stressed that men aged between 20 and 40 were most at risk. However, it was also said that those "on the slippery descent of middle age" were more likely to die once infected because they tried to "fight" the symptoms too hard instead of simply taking some quinine and going to bed.

The term 'Spanish influenza' rapidly took hold in Britain. The papers blamed the flu epidemic occurring there on the Spanish weather – their spring was dry and windy – an "unpleasant and unhealthy season" that saw microbe-laden dust being spread by the high winds. Therefore, the wet weather that most of Britain was subject to might stop the flu spreading there.

Many ordinary people had, due to World War I, become interested in foreign affairs and had read about the epidemic, discussing it with their friends and anticipating its arrival on British shores. Conspiracy theories abounded. Were the Germans carrying test tubes containing cultures from all known viruses and trying to infect other nations? Or was it the fault of Russia, the land of 'melodramatic mysteries'? The former theory was debunked at the end of June when the German army was affected by the epidemic and many soldiers were too ill to fight.

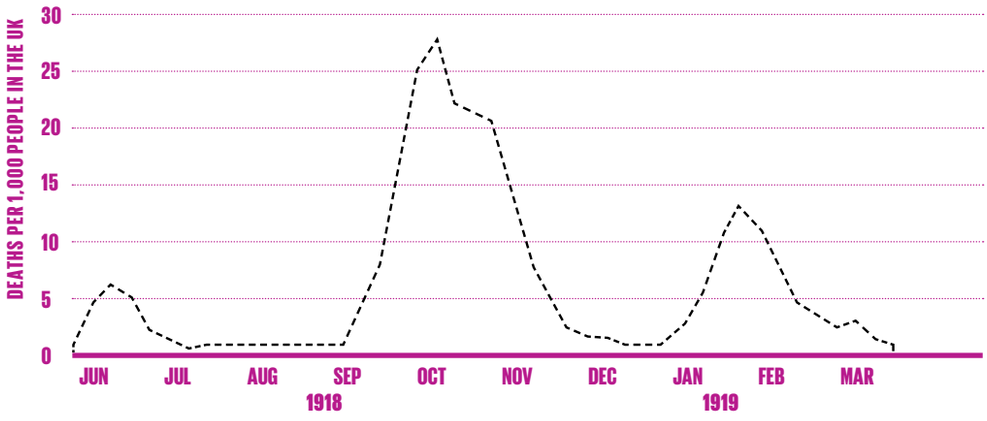
CONSPIRACY THEORIES

One of the side-effects of the virus appeared to be a deep depression, and this was seen to be a symptom that might have been conjured up by those wanting to destroy morale. One victim was reported as saying, "Well, it cures ambition," and this summed up the lesser-known dangers of becoming infected. Doctors were at a loss as to what to recommend to their patients; many urged them to avoid crowded places, or simply other people; other remedies included eating cinnamon and drinking wine or even Oxo's meat drink. Positives were sought. When it was reported that the Allies had experienced a good week on the front in France it was speculated that this might have been helped by the flu.

It was, perhaps, inevitable that conspiracy theories would spread – the British press was subject to censorship during this period of war, and if the seriousness of the flu pandemic had been recognised in the press early on, this might have affected the nation's morale. To stress the impact of the flu on the enemy, German forces had a useful propaganda effect, and so it was in the newspapers' – as well as the British Government's – interest to highlight only the 'foreign' cases. Spain, however, did not have press censorship and published freer accounts of the illness in its pages. This had the effect of making people erroneously think it was an illness specific to Spain, hence Spanish flu. The name stuck.

By 25 June 1918, it was recognised that the flu epidemic had reached Britain. At a meeting of the Hitchin Rural Council in Hertfordshire that day, the councillors heard that 600 cases had been reported at two different factories in Letchworth. The medical advice was to avoid going to cinemas and other crowded places and to keep the mouth and nose covered if going out. With cases mounting, a public notice was put in the British papers advising people of the symptoms, but it turned out that this was actually an advertisement for Formamints, a tablet made and sold by a company that also sold Sanatogen vitamins. The advert claimed the mints were the "...best means of preventing the infective processes" and that everyone should suck four or five of these tablets a day until they felt better. Even as people were dying there

FIGHTING INFLUENZA



was money to be made by advertising 'cures', especially as the medical profession seemed bereft of more practical ideas.

Once one person was infected, others quickly followed. In the Convent of Saint Vincent de Paul in Westminster, a 13-year-old girl died of the flu. She was believed to have infected 62 others in the convent. Two ten-year-old boys died in Deptford, with the coroner at their inquest suggesting that they should have rinsed their mouth and nostrils every morning with salt and water to avoid getting infected. In Birmingham, doctors said they were at their 'wits' end' and couldn't deal with the large number of patients. One doctor arrived at his surgery one morning to find nearly 200 people waiting to see him.

Manchester's dispensing chemists had to introduce a controlled queuing system because of the sheer number of people seeking remedies. The epidemic also hit in unexpected ways – one man due to be tried for bigamy at the Assize courts escaped prosecution because he came down with the Spanish flu. Whether he was too ill to attend court or the court officials were terrified of catching his illness is not known. Another man, Joseph Jackson, a discharged soldier who claimed to suffer from shellshock, was sentenced to six months in prison for GBH after attacking a police constable while drunk. His defence was that he had been suffering from Spanish flu and a friend had advised him that drinking beer would cure him.

GLOBAL PANDEMIC

The lack of healthy workers affected all areas of daily life. Council workers became gravediggers, railway workers made coffins, and ambulance drivers found that their vehicles were now hearses. As with previous historical disasters – the plagues that had haunted England in previous centuries, for example – pressure was put on services by the sheer rate of deaths and the impact of the flu on those who survived.

The epidemic had rapidly become a pandemic, making its way around the world. In August 1918, six Canadian sailors died on the Saint Lawrence River from a "...strange illness, which is thought to have been the Spanish influenza". The same month, cases were reported among the Swedish army, then its civilian population, and also among South Africa's labouring population.

The following month it reached Boston through its port, and by the end of October nearly 200,000 people in the US had died. Bodies piled up to such an extent it was said that families had to dig graves for their relatives. As a result of the widespread fatalities a serious shortage of farm workers developed, which affected the late summer harvest, and, as in Britain, other services, such as the collection of rubbish, were put under pressure due to a lack of staff.

As in Britain, Americans were offered conflicting and confusing advice. They were warned not to shake hands, to stay indoors, not to touch library books and to wear masks at all times. Schools and theatres were closed, and a Sanitary Code was issued that made spitting in the streets illegal. At one point, the use of aspirin was blamed for causing the pandemic, when it might actually have helped the ill. As a result of World War I, there was a shortage of doctors in some areas, and of those who were left, many became sick themselves. Makeshift hospitals were made out of schools and other buildings, and medical students had to take the place of some doctors.

Here, too, the flu virus hit people from all levels of society. President Woodrow Wilson was said to have been suffering from the flu while negotiating the Treaty of Versailles; Cawthra Mulock, described as "one of the very wealthy men of Toronto", died in New York in December 1918. 40 per cent of the US navy also became ill, and when four women sat down to a game of bridge one night, only one of them got up again the next day. It was estimated that some 28 per cent of the American population were infected. Elsewhere, the mortality rate was even worse. The pandemic spread to Asia, Africa, South America and the South Pacific, and in India the mortality rate was 50 deaths per 1,000 people.

By the spring of 1919 it was being reported that the numbers of deaths from the Spanish flu were decreasing. This did not mean it came to a quick end, however, and although the pandemic eventually died out, it did so only after attacking more than one-third of the world's population, leaving 50 million dead. It exposed the powerlessness of the medical industry, echoing what had happened during the Black Death. The Spanish flu was the last of the great plagues, and scientists are still striving to learn more about what happened to ensure history is not repeated.

Many workers wore masks on official advice to try to prevent catching Spanish flu from others

SPANISH FLU STATISTICS

12 YEARS

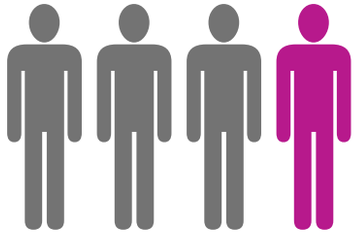
The amount American life expectancy dropped by as a result of the pandemic

10-20%

The mortality rate of those who were infected with the virus

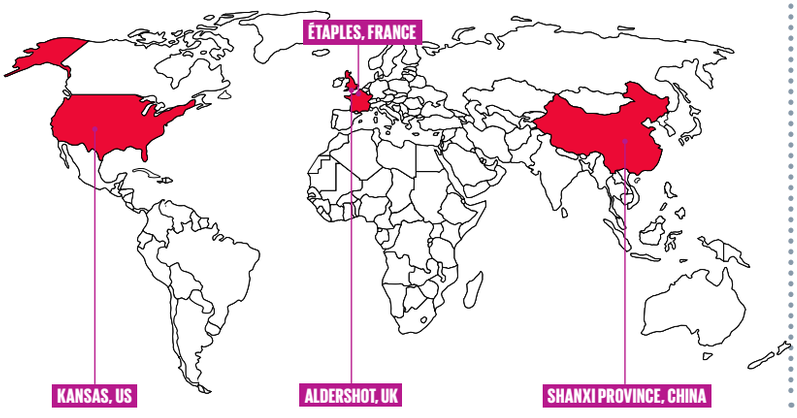
228,000

The number of people in Britain who died of Spanish flu



1 in 4 Americans were infected

4 POSSIBLE ORIGINS OF THE PANDEMIC



675,000

The estimated number of Americans who died

1/3

of the world's population may have been infected

2

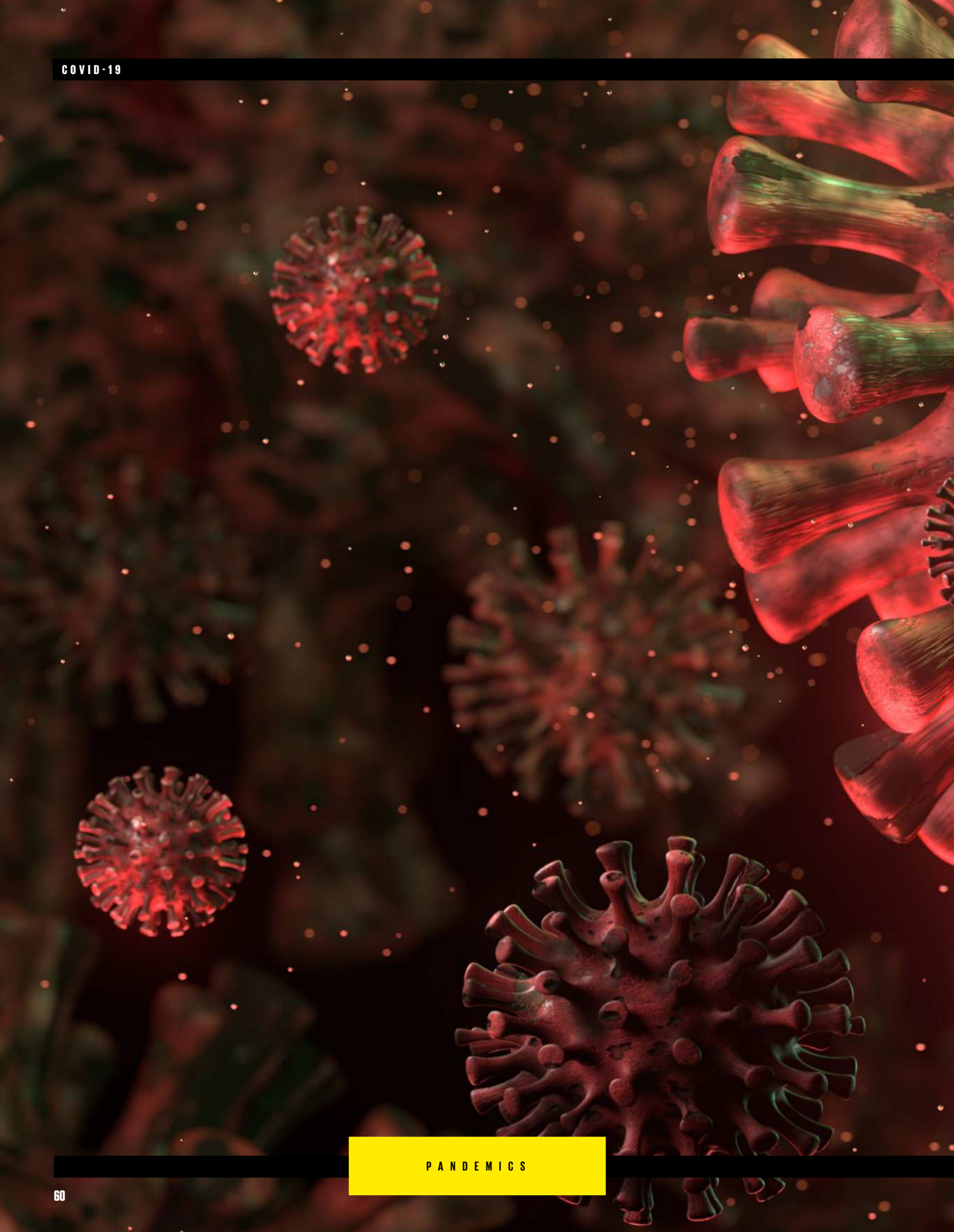
Years the pandemic was at its peak (1918–19)

3,000

The number of Chinese Labour Corps workers who got flu-like symptoms

50,000

Canadians died of Spanish flu



COVID-19

Prior to 2020, this virus was largely unheard of outside of scientific laboratories, but now it requires no introduction for almost nowhere on Earth has escaped its attention.

COVID-19, first identified in Wuhan, China, in December 2019, has, as of early January 2021, claimed nearly 1.9 million lives globally and infected over 87 million people.

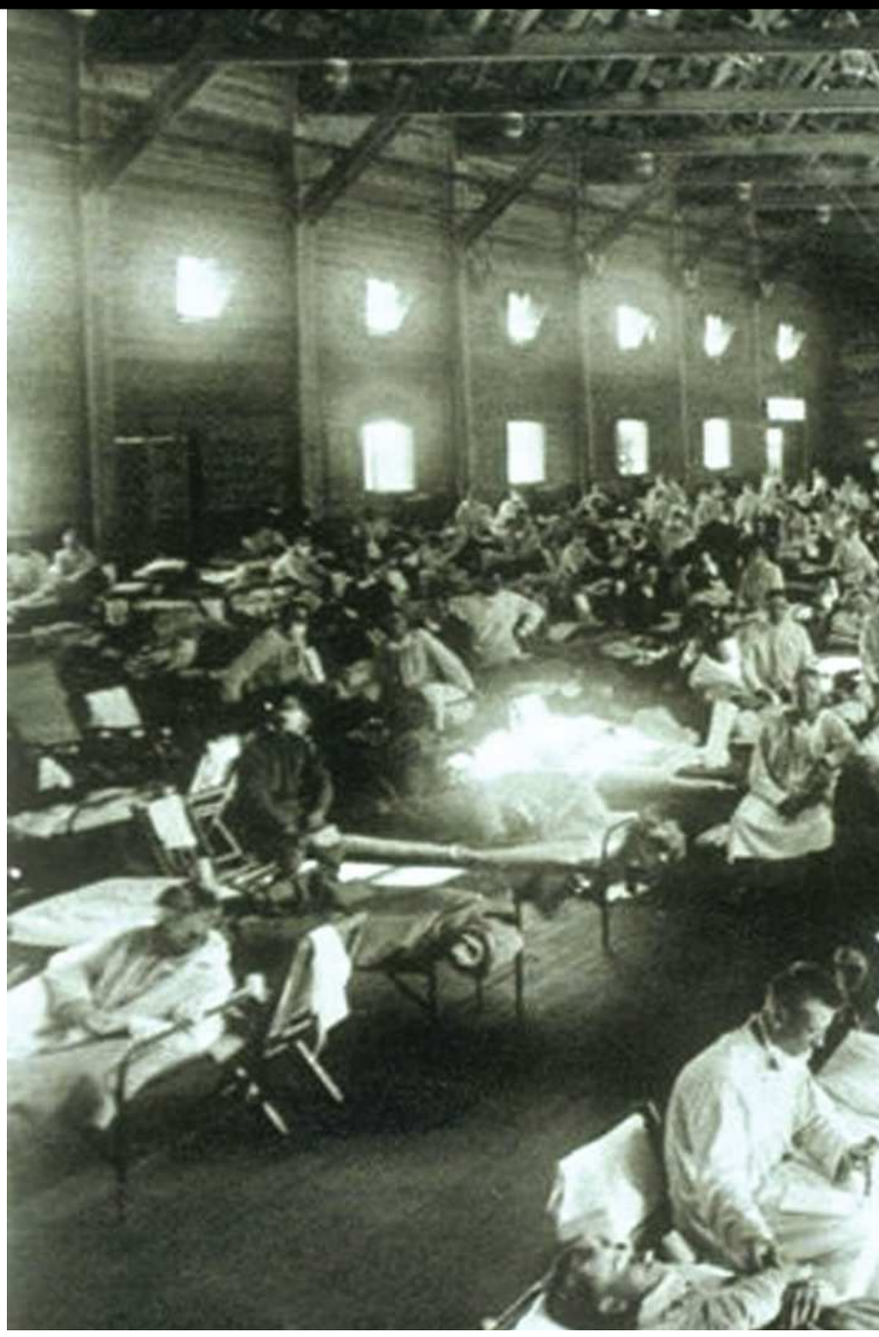
The national lockdowns and lifestyle restrictions imposed to try to combat the spread of the virus have been effective in reducing cases, but according to the International Monetary Fund (IMF) the economic impact of measures imposed to slow contagion will be a £21.5-trillion ($28-trillion) loss in global output.

There is no doubt that the personal and financial devastation wrought by COVID-19 will leave deep scars, and recovery will take many years, but the rollout of a number of vaccines should bring the virus under control in the months ahead, perhaps heralding a return to normal life before the end of 2021.

A US ARMY MEDIC FIGHTING SPANISH FLU

UNITED STATES, OCTOBER 1918

With approximately 5 million US military personnel drafted during World War I, crowded army camps and trenches were a breeding ground for a deadly wave of influenza known as Spanish flu. At the height of America's involvement in the conflict, Spanish flu infected up to 40 per cent of the army and navy, diminishing the active troops in their tens of thousands. Pressure on medics increased to treat a virus that had developed a hardy immunity to previous methods of treatment. Despite the medics' best efforts, by the end of the war more troops had died from influenza than in battle.



ADMISSION

The hospital tents, which had been separated from the general casualties of war, were overcrowded and overstretched, and admitting new patients was a lengthy and laborious task. To give an idea of the rate of the admission, the US Navy recorded a total of 106,000 hospital admissions by the end of the war due to influenza and pneumonia.

MAKING THE ROUNDS

Pressure to get troops back onto the battlefield was high, and the line officers were more concerned about those well enough to fight as opposed to those still sick. But when it was time for the medical department to check on the patients, few, if any, had made a full recovery.

TREATMENT

As the sickness spread, medical officers sprayed the mouths and throats of 800 patients each day with a solution called dichloramine-T as a preventive measure. Unfortunately, when they compared influenza rates among untreated men, the medics found the treatment made little to no difference.

©Wiki

EXAMINING THE DEAD

In a bid to understand more about the newer and deadlier wave of influenza, autopsies were performed on the recruits that died. Hoping to find answers, there were often more new questions than revelations as to why the disease was killing off what were formerly fit and healthy young men. The reports on their findings formed some of the most extensive research into the virus that has ever been produced.

DECISION TIME

Quarantines were almost impossible to maintain and medics often found themselves arguing with army officials about isolating patients when they needed to ship them to Europe on crowded vessels. Medical personnel advised against the transportation of soldiers but, as the war raged, army officials were eager to send men to the front lines to fight, knowing full well that the pandemic was in full swing.

CONTACT RELATIVES

Because so many individuals became seriously ill, camp officials were routinely sending out 'danger' or 'death' telegrams to families and loved ones. Because they received so many return calls, telegrams and visitors, the army had to set up a separate hospital tent as an information bureau to direct the flow of traffic regarding the sickly and the deceased.

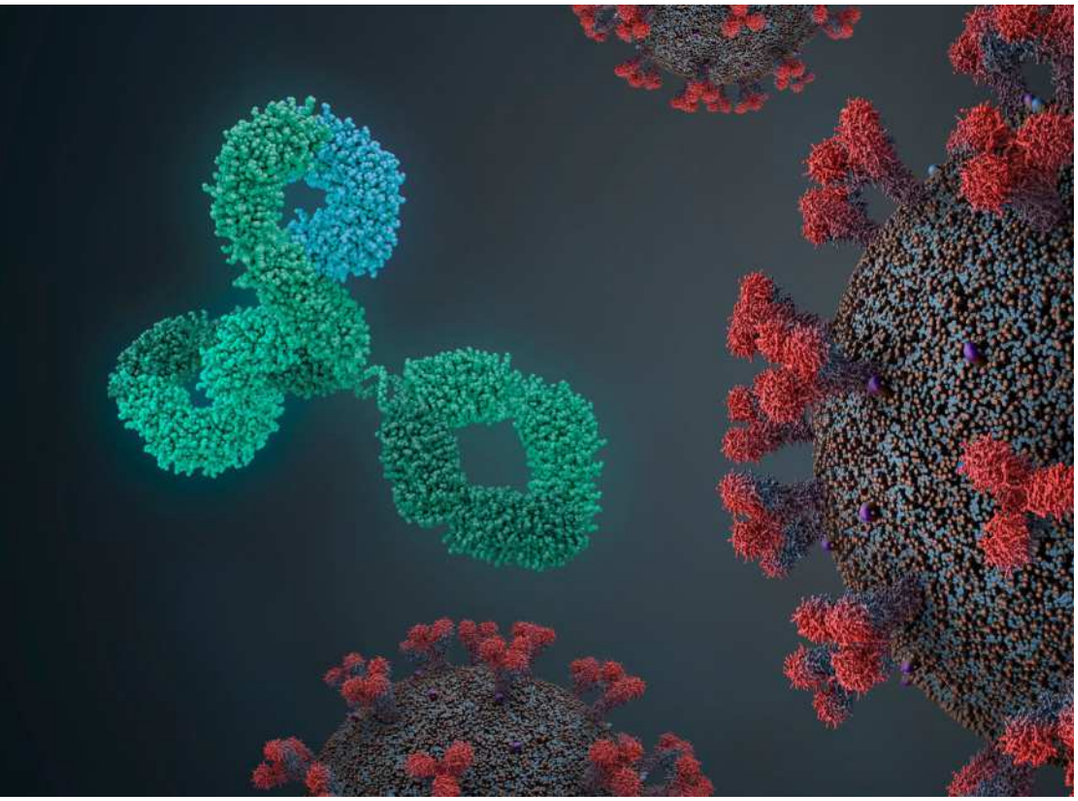
REMOVE THE BODIES

With fatalities rising at an alarming rate, a standard mortuary, which was only built to deal with four bodies at a time, would quickly become overcrowded. Officials negotiated with local undertakers to take the bodies for $50 each. When a flatbed truck was produced to remove the dead, the army quickly provided more dignified closed trucks to transport the bodies in.

REST, RECUPERATE, REMEMBER

After a long day of treating patients, the medics would need to rest themselves, although sleep and peace of mind were often slow to come after seeing men squirming and writhing as death took hold. However, due to pure exhaustion, they would eventually succumb to sleep before starting again the next day.

A symptom of the 1957 pandemic for young boys was nose bleeds



The virus that caused the 1968 pandemic jumped species into pigs and crossed back again in the form of 'swine flu'

THE FLU OUTBREAKS OF '57 AND '68

WITH THE WORLD CURRENTLY IN THE THROES OF A CORONAVIRUS PANDEMIC, WE EXPLORE HOW IT COMPARES TO THE INFLUENZA PANDEMICS OF 1957 AND 1968

WRITTEN BY **JOSIE CLARKSON**

In 1957 and 1968 the world succumbed to violent flu outbreaks. Every year the flu season occurs with its fair share of casualties, so what was so special about the flu in those two years that catapulted it to pandemic status, and how did we manage to overcome it?

The influenza virus is an airborne virus that causes symptoms of fever, aches across the body and fatigue collectively known as the flu. The virus has two proteins on its surface, known as antigens: hemagglutinin (HA) and neuraminidase (NA). These antigens are what the body's immune system reacts to, triggering an immune response. Once someone has been exposed to a virus their immune system makes corresponding antibodies that exactly match the antigens on the virus so it can be easily recognised if the individual is infected again.

However, viruses have a trick up their sleeves to evade detection. Their antigens can mutate to change shape in a process called 'antigenic drift'. These small changes accumulate over time until they are different enough that the antibodies no longer recognise them and the learnt immunity fails. An even more dramatic change in the antigens is caused by 'antigenic shift', whereby a human and an animal version of a virus swap some of their genes, creating a new subtype that can infect both species. When this happens the human population has no immunity against the new virus and a pandemic can occur.

This happened in 1957 when a new strain of the influenza virus emerged as a combination of influenza strains from birds and humans. The new virus was the H2N2 influenza subtype,

SANS FRONTIÈRES

AN INFECTIOUS DISEASE THAT SPREADS RAPIDLY THROUGH A COMMUNITY IS AN EPIDEMIC. IF THAT DISEASE SPREADS TO COUNTRIES ACROSS THE WORLD, IT BECOMES A PANDEMIC

THE 1957 PANDEMIC KILLED

20,000
PEOPLE IN THE UK

116,000
PEOPLE IN THE US

1 MILLION+
PEOPLE WORLDWIDE

THE 1968 PANDEMIC KILLED

30,000
PEOPLE IN THE UK

100,000
PEOPLE IN THE US

1-4 MILLION
PEOPLE WORLDWIDE

with the letters and numbers corresponding to novel versions of the HA and NA antigens. The first cases of the virus were reported in China in February 1957 and, by April of that year, a major epidemic was declared in Hong Kong, with a quarter of a million people infected. The virus quickly swept across the world, causing an estimated 9 million infections in the UK.

Despite this onslaught, no measures like social distancing were put in place to protect people, and there was very little coverage in the media. Industries like factories, offices and mines had to close due to staff absences, and without the facilities we have today to enable home working, countless businesses ground to a halt. Plus, UK regulations forced infected individuals to go to their GP for a doctor's note before they were entitled to sick pay. This rule put enormous strain on the health system as so many healthcare workers succumbed to infection. Over in the US, officials were encouraging people not to visit their doctor, which helped to limit the spread of infection and the impact on the health system.

Usually, the influenza virus weakens the body, making it susceptible to attack by other pathogens, like bacteria, that cause pneumonia. However, this virus was especially destructive because, unlike previous strains, it was lethal by itself without the need for a simultaneous bacterial infection. Intensive care units didn't exist in 1957 and only very basic ventilator equipment was available, so people with underlying heart or lung conditions could often not be saved. Individuals with rheumatic heart disease and heavily pregnant women were among the most likely to die from the virus.

"THE H2N2 VIRUS TARGETED YOUNGER GENERATIONS. PEOPLE OVER THE AGE OF 65 HAD IMMUNITY THANKS TO A SIMILAR STRAIN THAT CIRCULATED IN THE LATE 1800s"

What was even more terrifying about the H2N2 virus is that it seemed to preferentially target younger generations, 49 per cent of whom were between just five and 14 years old. It was later discovered that people over the age of 65 were less vulnerable as they had some immunity to this new virus thanks to a similar influenza strain that circulated in the late 1800s. The general symptoms were not dissimilar to previous flu strains, except that young boys who were infected seemed to experience the curious symptom of nose bleeds.

After the first phase of the virus over the spring and summer months, the second – and more devastating – phase hit in autumn, coinciding with children's return to school. However, scientists were fighting back thanks to the quick thinking of microbiologist Dr Maurice Hilleman. Within three weeks of the initial outbreak in China, Dr Hilleman had acquired samples of the H2N2 virus for his lab in Washington, DC. Working with researchers in Melbourne and London, a vaccine was developed at an unprecedented rate that restricted the pandemic-inducing virus to a mere seasonal flu strain.

Unfortunately, by the time the vaccine arrived, estimates suggest more than a million people had lost their lives to the H2N2 influenza virus. And it didn't end there. During 11 years of seasonal attacks the virus underwent antigenic drift, eventually mutating into the H3N2 virus and causing a new pandemic in 1968. In this new strain, the HA antigen had changed beyond all recognition, but the NA antigen remained the same as it had been in 1957.

The H3N2 virus began in Hong Kong in July 1968, exploding into half a million cases in just two weeks. This novel strain was extremely contagious, and by September it had reached the US. It made this vast journey across the Pacific inside American troops returning home from the Vietnam War.

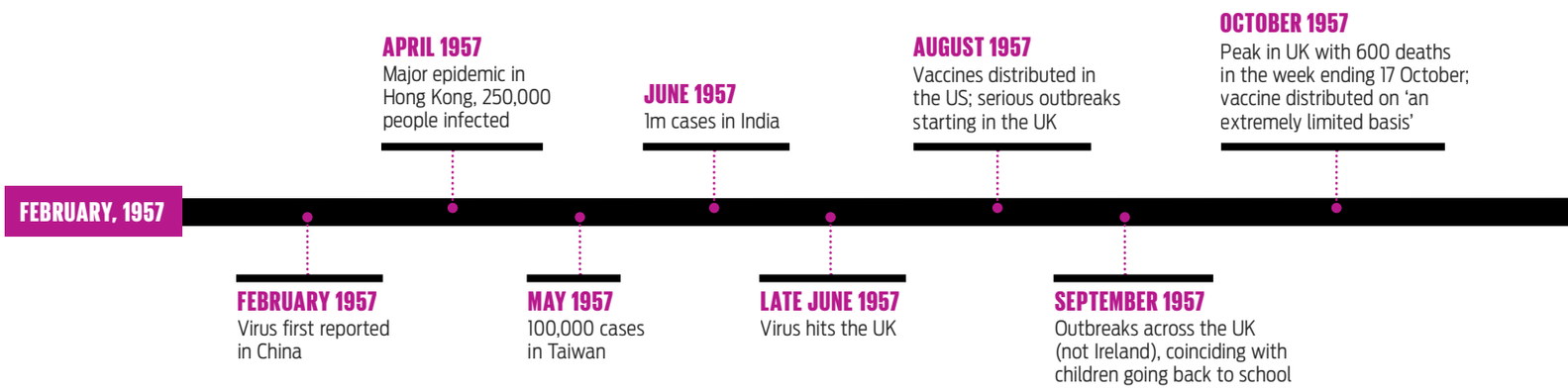
Far from being a repeat of the 1957 pandemic, this time the severity and pattern of the virus varied significantly between countries and individuals. In Japan, for example, small pockets of epidemics initially occurred randomly across the country until the end of 1968. By contrast, the US experienced countrywide rocketing rates of infection and death from the new strain over the winter, reaching its peak in December and January. In Western Europe, the story was different again. Although much of the population was infected, the death rate was significantly lower than in the US and below the levels seen during the 1957 pandemic.

What was the reason for this wide range of effects? Having been hit hard in the last pandemic, many Asians and Europeans had built up some level of immunity to the NA antigen, which is common to both the H2N2 and the N3N2 influenza strains. Plus, for this same reason, the H2N2 vaccine was roughly 50 per cent effective against this new strain. Aside from this vaccine, there were no social interventions to try to limit the spread of the virus. Again, businesses suffered due to a threadbare workforce, especially the postal and rail services.

The immunity from the last pandemic didn't protect people for long. By the 1969-1970 flu season, the NA antigen on the H3N2 virus had mutated slightly. While it did not change enough to constitute a new influenza subtype, it was sufficient to infect people who'd resisted it the previous year thanks to their immunity to H2N2. As with the H2N2 strain, the symptoms present

The 1968 pandemic was believed to have originated in Hong Kong, earning it the nickname 'the Hong Kong flu'

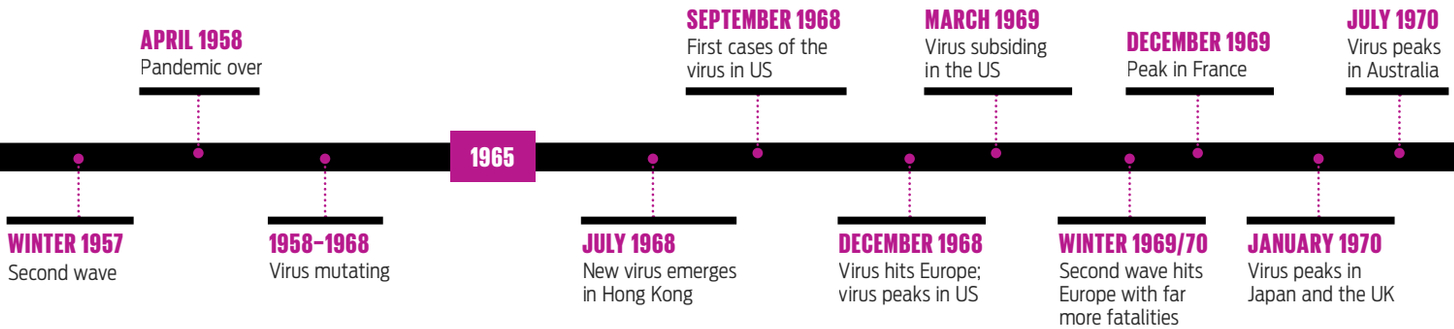
TIMELINE FROM 1957–1970



were the usual flu symptoms, and most people only experienced a mild form of it. In fact, a study by the Royal Air Force found that roughly half of people who had been infected with H3H2 did not experience any symptoms. But many were not so lucky: some estimates suggest as many as 4 million lives were lost, with the highest levels of mortality seen in infants and the over-65s. A vaccine was eventually developed to combat the H3N2 strain, but it was largely redundant as it didn't come until after the pandemic had peaked in many countries.

Although the H2N2 strain of influenza virus that caused the 1957 pandemic has now disappeared, having morphed into the H3N2 strain, this new strain - which caused the 1968 pandemic - returns every flu season. It is now the strain of seasonal influenza that causes the most illness and death each year. Worse still, evidence emerged in 1990 that H3N2 has jumped the species barrier into pigs. This is concerning because experts believe that the virus can mutate slightly in pigs before returning to the human population. In fact, this happened in 2009, resulting in the widely publicised 'swine flu' scare, which, thankfully, never lived up to the deadly potential the media had predicted.

Perhaps this false alarm contributed to the public's hesitancy to react to the novel coronavirus strain that hit the news in early 2020. Although there are some similarities between coronavirus and influenza, they are distinct viruses. However, lessons can be learnt from the handling of the influenza virus pandemics of 1957 and 1968. Many government bodies have implemented travel restrictions and business closures to try to control the virus, but, with several vaccines on the horizon, there could be a swift end to the current coronavirus pandemic, similar to the demise of the 1957 influenza pandemic.



INSIDE THE FLU

WE REVEAL HOW THIS COMMON WINTER BUG STAYS ONE STEP AHEAD OF OUR IMMUNE SYSTEM

The influenza virus infects a staggering 5 million people worldwide every single year, travelling from person to person in airborne droplets and causing chills, fever, a sore throat, a runny nose, headaches and muscle pain.

The flu virus changes gradually by a process known as antigenic drift. As the virus replicates, single nucleotide errors occur in the viral genome, causing minute changes to the proteins that coat the outside of the virus. The immune system detects and destroys these proteins, but as they change, the ability of the body to recognise the virus decreases, preventing people from building up immunity.

Not only does the virus make continual, subtle changes to its genome and proteins, but it also occasionally develops huge mutations. If a host becomes infected by more than one strain of flu virus, and the two meet inside a single cell, there is a chance that their genomes will mix together, consequently producing a new, mutant flu virus. This is a rather rare occurrence, but it can form dangerous new strains of flu. The swine flu (H1N1) pandemic of 2009 was found to contain genetic information from four different viruses: one human, one avian and two swine influenza.

This is one of the reasons that a universal vaccine against all types of flu is proving to be such a challenge for science to overcome. Currently, a seasonal flu jab is developed every year, to match the flu that is circulating in the population. Each subsequent year, the virus has usually changed sufficiently that the vaccine is no longer effective.

However, new research suggests that some cells of the immune system can recognise proteins from the core of the virus. These are essential to viral function and mutate far more slowly, so developing a vaccine against these important proteins could help T-cells to develop long-term immunity to the bug.

GET TO KNOW YOUR ABCS...

INFLUENZA A

The natural hosts of influenza A are wild water birds. Transfer to domestic poultry exposes humans to the virus and can result in cross-species infection. The H1N1 Spanish flu of 1918 and the H5N1 bird flu of 2004 were influenza A.

INFLUENZA B

Influenza B prefers a human host and is less common. It mutates slowly, enabling most to build up immunity, but it doesn't last forever. It rarely infects other species, thereby preventing the creation of the new, mutant strains that cause pandemics.

INFLUENZA C

This produces only mild disease, and most adults have been infected at some point in their life. It infects humans and pigs, but is far less common than influenza A and B. It can cause local epidemics, but does not lead to pandemic flu.

THE VIRUS IN FOCUS

TAKE A CLOSER LOOK AT THE ANATOMY THAT MAKES UP A SINGLE FLU VIRION

RNA

The genetic material of the flu virus is stored on several strands of ribonucleic acid (RNA).

HAEMAGGLUTININ

Spiky protein haemagglutinin coats the outside of the virion, allowing it to stick to, enter and infect cells of the throat and lungs.

MATRIX

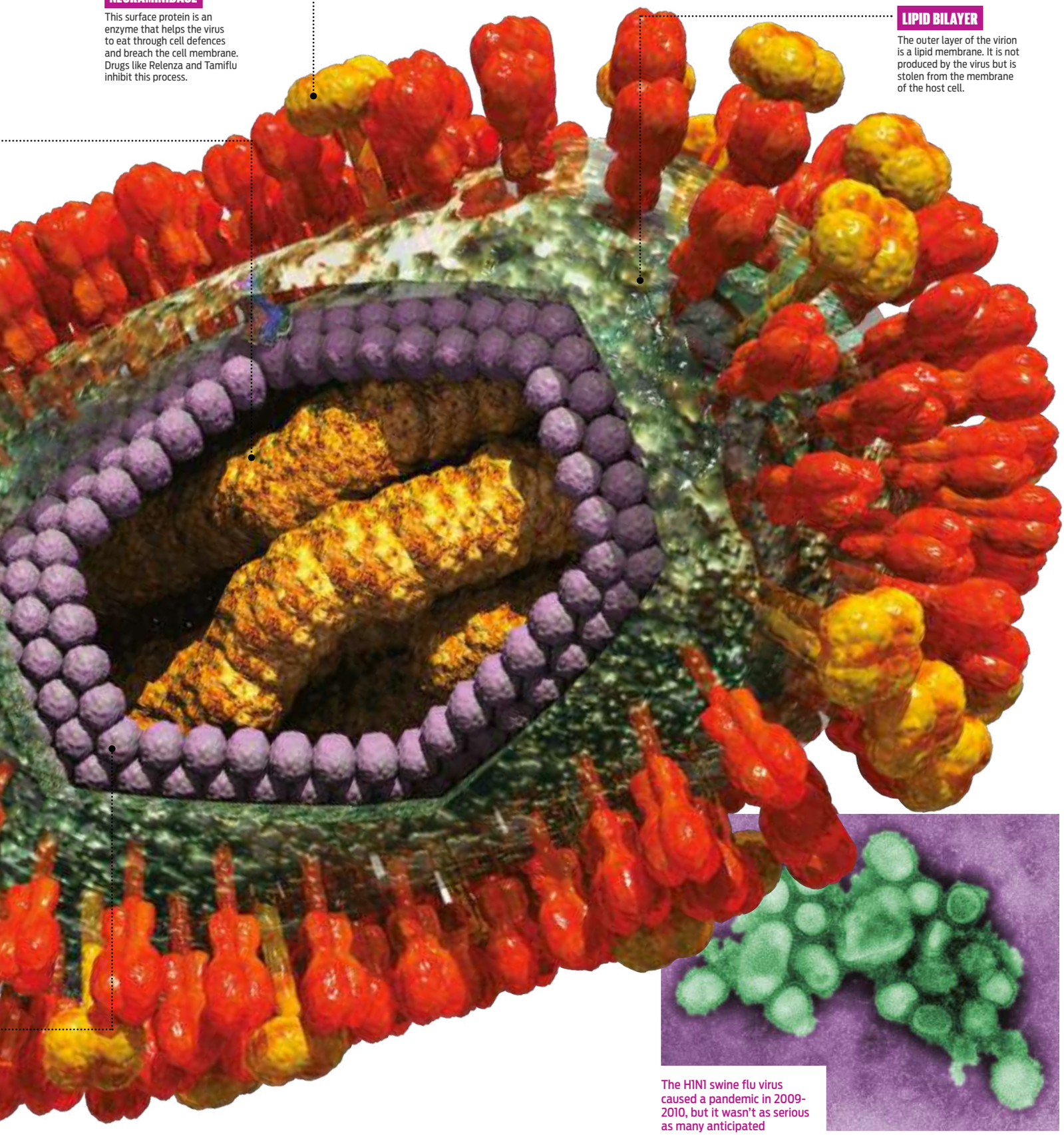
Beneath the membrane is a protein shell, which provides the virion with strength and structure.

NEURAMINIDASE

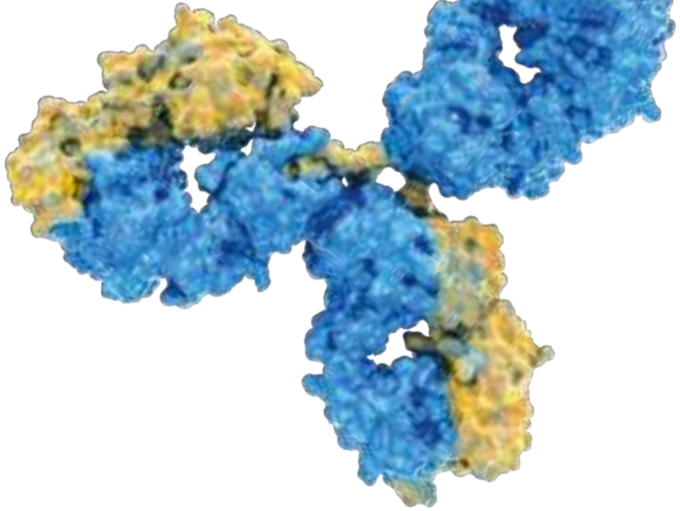
This surface protein is an enzyme that helps the virus to eat through cell defences and breach the cell membrane. Drugs like Relenza and Tamiflu inhibit this process.

LIPID BILAYER

The outer layer of the virion is a lipid membrane. It is not produced by the virus but is stolen from the membrane of the host cell.



The H1N1 swine flu virus caused a pandemic in 2009-2010, but it wasn't as serious as many anticipated



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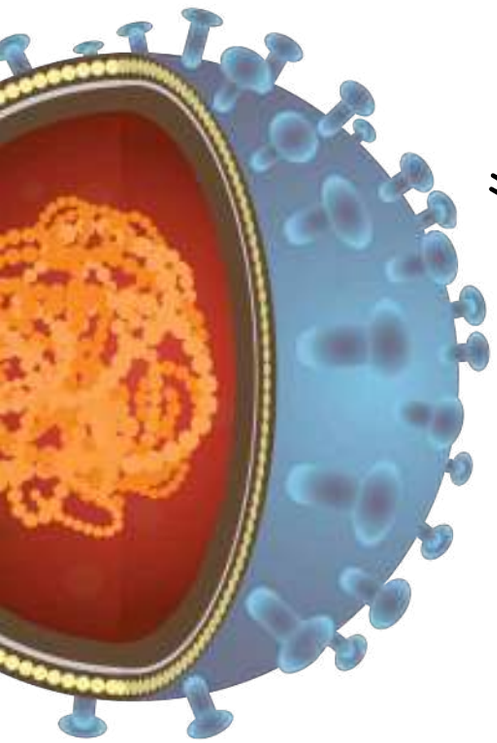
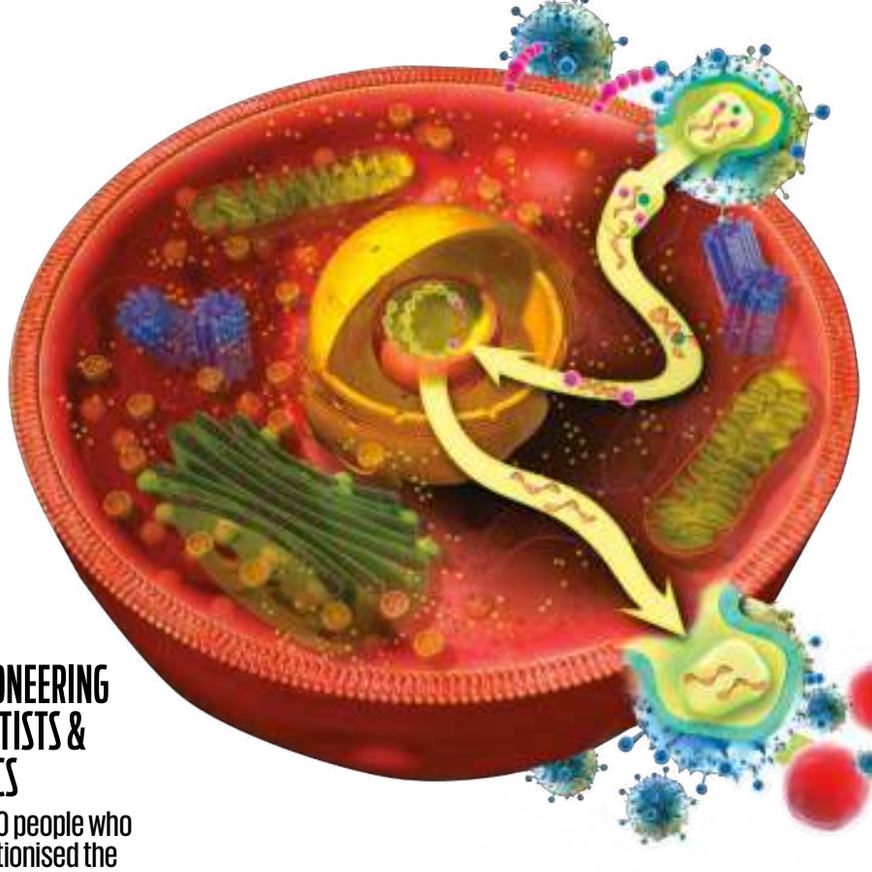
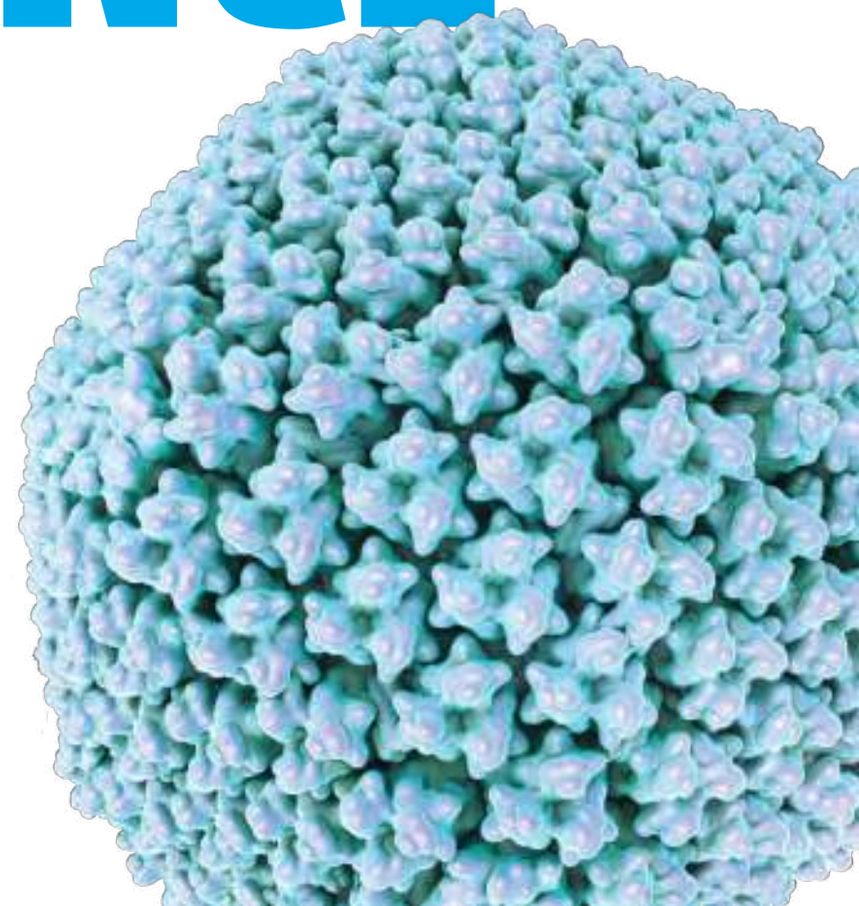


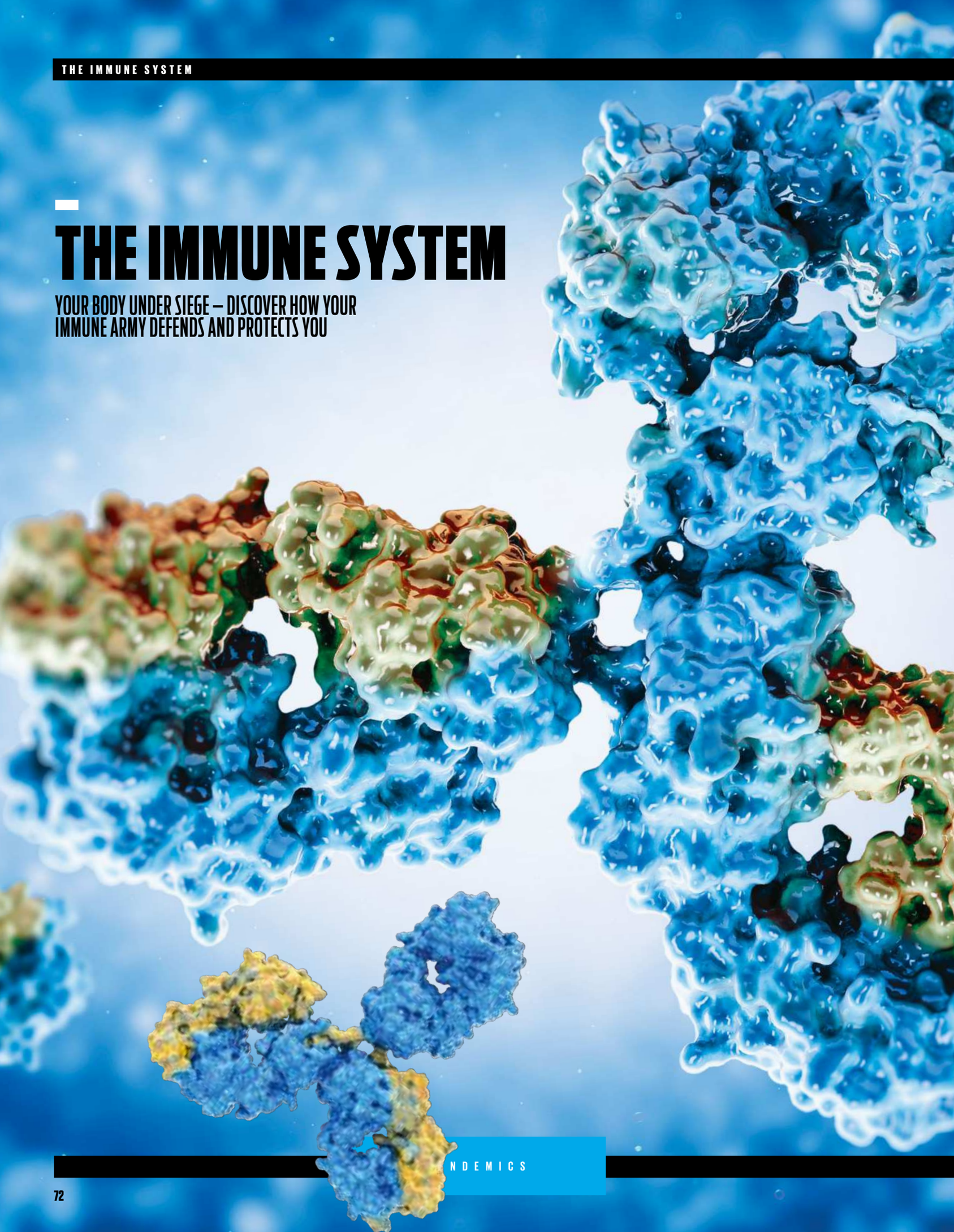


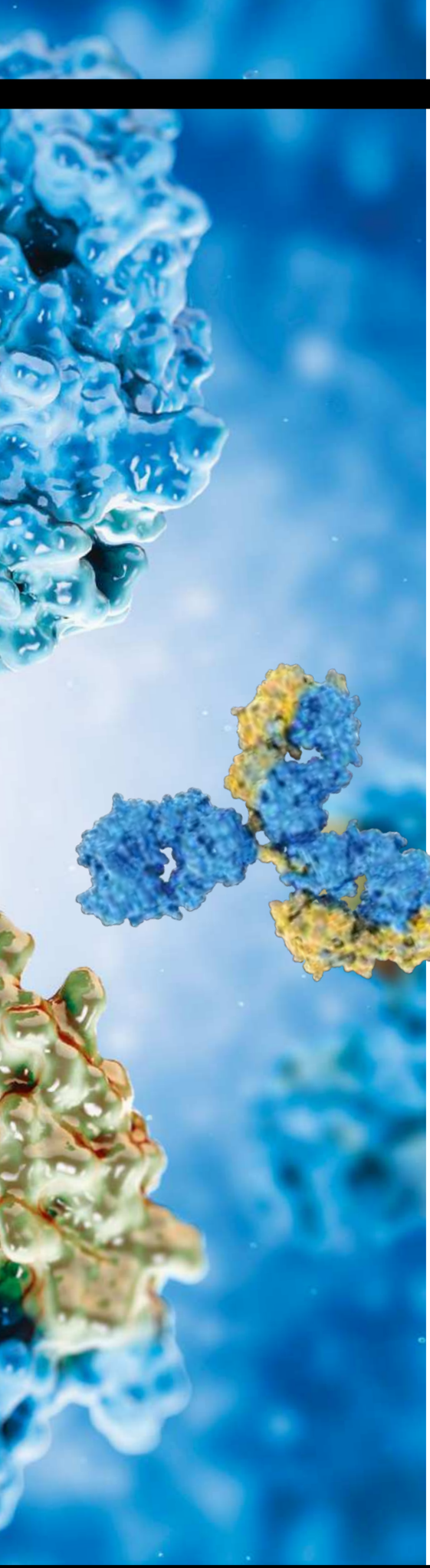
SCIENCE



THE IMMUNE SYSTEM

YOUR BODY UNDER SIEGE – DISCOVER HOW YOUR IMMUNE ARMY DEFENDS AND PROTECTS YOU





From cleaning the kitchen sink to having sex, everything we do exposes us to invaders. Yet we are safe. Most of the time potential invaders' attempts are thwarted. This is because the human body is like an exceedingly well-fortified castle, defended by billions of soldiers, and I'd like to reveal its myriad of miracles and secrets to you.

THE DARK ARTS OF THE INNATE DEFENCES

Our story begins with a feat of imagination: if we were to put 100 people in a room, hand them some crayons and ask them to draw a defence system, what might you expect to see? You can have a pretty good guess – probably castles with high, impenetrable walls surrounded by moats (shark-infested, among the more creative participants). A less historically inclined artist might draw us an array of lasers, rockets and machine guns.

These are relatively predictable because even without knowing what you're defending against, there are certain solid choices you can make. This is akin to the 'innate' arm of the immune system – the set of defences that we are born with and which essentially remain the same throughout our lives.

The innate system is the first line of defence because it's already set up and ready to take on a range of common pathological patterns. For instance, all invaders need an entry point – it doesn't matter if you're a tiny virus or a massive worm, you need a way in – so part of the innate immune system's role is to maintain robust control of the body's entry and exit points.

Cue our first innate defence: skin. Skin is the largest human organ; if you were to peel yours off you'd lose about 12 kilograms instantly. The skin on the soles of your feet is eight-times thicker than the skin on your eyelids, but every inch of it is a barrier that keeps invaders out.

While snakes shed their skins in one go, we slough off old skin continuously and rain it down at a rate of roughly 50,000 cells a minute. Given that fact, it's almost unsurprising that dead skin accounts for about a billion tons of dust in the atmosphere. Unsurprising, but gross. On the plus side, this constant turnover of cells means the barrier is continually replenished, keeping our skin healthy and keeping the billions of bacteria slathered over its surface out.

Unfortunately, we can't be truly impenetrable. We need to let in food and water and air and light, and we need to let some things out, too. So we have a body full of holes, which is deeply inconvenient from a security perspective. But we have clever holes. Take your mouth: every time you inhale you are sucking about 10,000 bacteria into your lungs. Thankfully, your airways are exceedingly well booby-trapped passages lined with goblet cells, which secrete a fine layer of mucus to trap dirt and bacteria. The dirty mucus is then escorted out by microscopic whip-like structures called cilia, which stick out from the lining of the airways and beat 1,000-1,500 times per minute, forcing the mucus up and out of the lungs in waves at a rate of two to three centimetres per minute.

While the lung escorts invaders out in an orderly fashion, the gut takes a more medieval approach to border control: acid. This acid is the reason the normal stomach is an unwelcoming pH 2, capable of disintegrating many of the microorganisms that land in it. The discovery of this acid has a rather gruesome history.

The story begins in June 1822 on the island of Michilimackinac in the wilds of Michigan, US. At the time this lush green island, christened 'the great turtle' by the native Ottawa and Chippewa tribes, was the main trading post of the American Fur Company (the brainchild of America's first multimillionaire, John Jacob Astor, who died during the 1912 sinking of the Titanic).

AN EPIDEMIC OF ALLERGIES

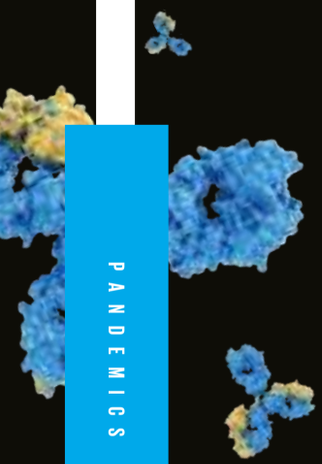
Do you have any allergies? If so, you're not alone; according to Allergy UK, "More than 150 million Europeans suffer from chronic allergic diseases, and the current prediction is that by 2025 half of the entire EU population will be affected."

90 per cent of food allergies are caused by just eight things: milk, eggs, peanuts, nuts from trees, fish, shellfish, soy and wheat. All of these allergies are caused by the immune system reacting to a harmless substance by launching an unwarranted attack that can cause symptoms from a rash to a life-threatening airway blockage.

While we don't know why the immune system does this, we do know some people are more genetically susceptible to allergies because they run in families.

YOUR IMMUNE SYSTEM

DISCOVER SOME OF THE DIFFERENT ORGANS AND COMPONENTS THAT MAKE UP YOUR BODY'S DEFENCES



TEARS

Our tears contain antimicrobial chemicals including lysozyme, lactoferrin and lipocalin to protect our eyes from microorganisms in the environment.

EARWAX

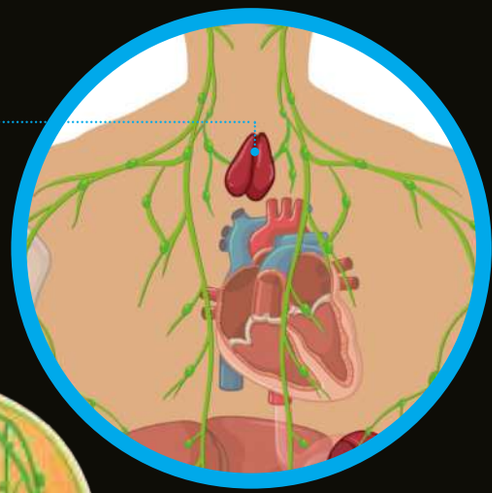
Earwax is an innate immune defence as it carries detritus out of the ear and contains microbe-killing chemicals.

LYMPH NODES

This is where special white blood cells can be presented with foreign material like bacteria and set off to kill it.

THYMUS

A gland whose size peaks during puberty then shrivels. It's where T-cells, a type of white blood cell, mature.



The immune system is critical to the success or failure of organ transplants

SPLEEN

This removes old red blood cells and is rich in white blood cells called splenic microphages.

INTESTINE

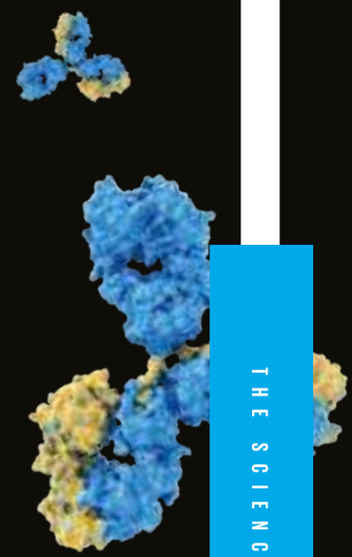
Contains Peyer's patches, tissue that can act like an alert system for detecting intruders in the gut.

SKIN

Skin is an essential part of the immune system, keeping potentially dangerous microbes out.

LYMPHATIC VESSELS

An unidirectional transport network that's a key way for white blood cells to travel the body.



"WE MAKE MORE ANTIBODIES THAN THERE ARE STARS IN OUR GALAXY"

Skin is an essential defence, keeping out a multitude of microbes

David Vetter lived life in a bubble because he didn't have an immune system to defend him

"THE IMMUNE SYSTEM INFLUENCES EVERYTHING FROM PREGNANCY TO ORGAN TRANSPLANTATION"

It was while standing in line at the Fur Company store that a 20-year-old trapper by the name of Alexis St Martin was accidentally shot. The only doctor on the island arrived to a scene worthy of any horror movie: 'A portion of the lungs as large as a turkey's egg protruding through the external wound.' St Martin also had a hole in his stomach through which his breakfast was spilling out on to his shirt. His doctor, an army surgeon by the name of Beaumont, thought St Martin had little chance of survival, but astoundingly, with the care of Beaumont, St Martin slowly became whole again. Well, almost. The hole in his stomach didn't fully heal, and St Martin declined offers from Beaumont to stitch it shut. This physical quirk changed the history of science.

Over the course of several years and 238 experiments, Beaumont extracted acid and introduced medicine and food into the hole in St Martin's stomach. This led to Dr Beaumont's seminal publication on the subject, including conformation that hydrochloric acid is the most important acid in the stomach.

ADAPTIVE ASSASSINS

Let's imagine a different task from our original artistic efforts. If we had given our 100 people the challenge of drawing a defence system against a very specific threat, they would have drawn rather different defences. For instance, garlic and holy water would be essential in an anti-Dracula defence system but would be frankly embarrassing in the face of Darth Vader. This opponent-specific weapons selection resembles the 'adaptive' arm of our immune response, which complements the breadth of the innate response by being able to recognise and respond to specific threats.

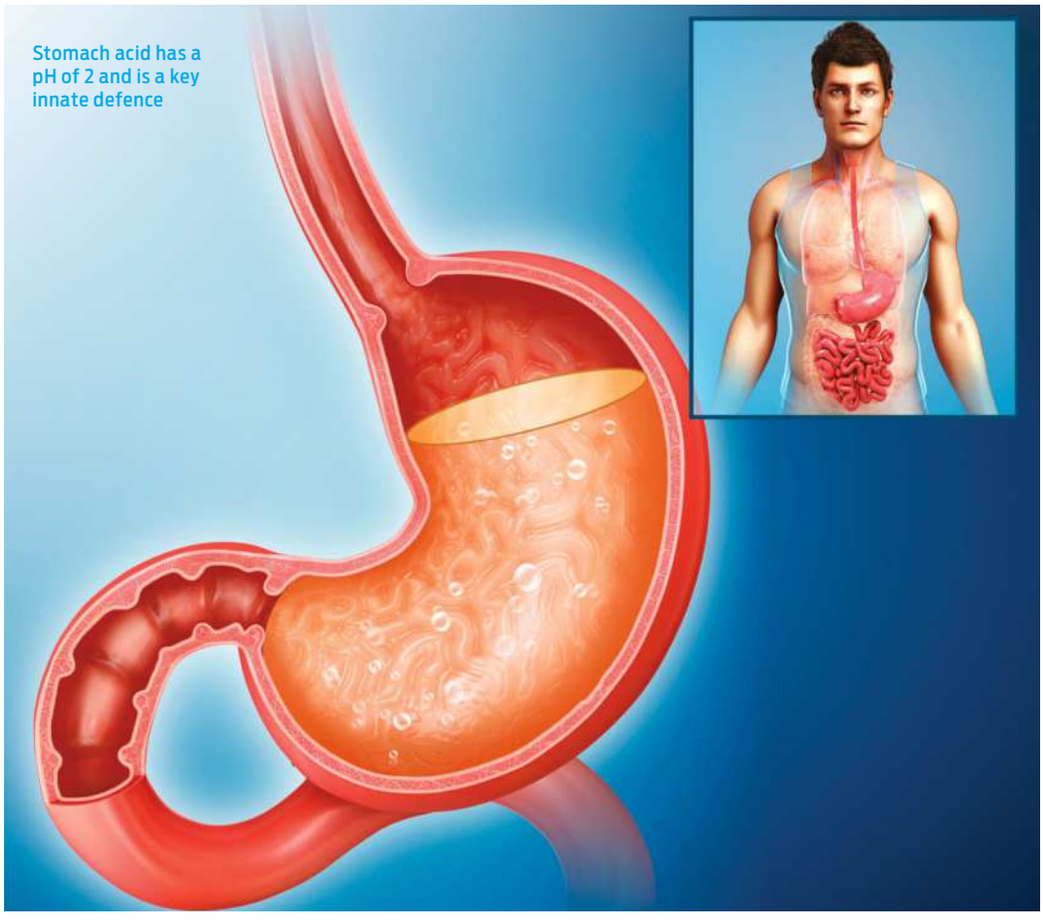
Included within the adaptive system are antibodies, which are Y-shaped proteins that can latch onto bacteria, parasites and viruses and

AUTOIMMUNE DISEASES

Sometimes, the immune system turns on the very body it's designed to protect. We don't know why, but white blood cells can fail to recognise the body's own cells as belonging to it. The classic example is type 1 diabetes, where the immune system attacks the pancreas.

By systematically destroying the beta cells of the pancreas, the immune system renders the body incapable of making insulin, a hormone essential to controlling blood sugar levels. A diabetic person must use frequent blood tests and synthetic insulin to reduce the risk of serious consequences, including going blind or needing to have limbs amputated.

The severity and commonality of this disease is inspiring many innovative solutions, including in the US, where a bionic pancreas is currently under development.



Stomach acid has a pH of 2 and is a key innate defence

IMMUNOLOGY, SEX AND DEATH

Pity the poor male brown antechinus, a small marsupial found in southeast Australia. In preparation for the short breeding season he stops making sperm and his testes disintegrate, leaving him with stores of sperm and a need to procreate. And so he does, spending up to 14 hours a day mating. But all this comes at a cost in the form of massively raised levels of cortisol, a stress hormone.

High cortisol leads to severe suppression of immune messenger chemicals, which means that when a male brown antechinus gets injured or ill it can't mount an immune response. This ultimately leads to the death of our valiant, virile little friend.

The male brown antechinus goes on a mating frenzy that ultimately ends in his demise

label them for destruction by our white blood cells, which then eradicate the threat.

Our ability to make a diverse array of antibodies is legendary. We can make over 1 trillion different antibodies – that's more antibodies than there are stars in our galaxy. Generating this level of diversity means that, given enough time, our body can develop antibodies against everything from the common cold to the Black Death.

Alas, sometimes infections move too quickly and kill us before we have a chance to develop tailored antibodies. Other infections change their shape to evade our adaptive immune response. HIV is well known for it's ability to mutate, changing its surface shape and making it exceedingly difficult for our immune system to make new antibodies quick enough to adapt to HIV's changing face.

TRANSPLANTS

The immune system not only defends and protects us; it also plays a key part in a range of life experiences, from pregnancy to organ transplantation. For example, research suggests that the immune system may play a crucial part in whether a fertilised egg safely implants into the womb and therefore whether a pregnancy is able to proceed normally or tragically ends in a devastating miscarriage.

In the example of transplants, our immune system can recognise the new organ as foreign and damage it until it can't function, a process called rejection. One option to attempt to avoid transplant rejection is to use cells from the recipient's own body, known as 'self-cells', because the immune system won't see the new tissue as foreign and attack it.

For instance, people who lose a thumb can understandably struggle with using their hand. Some therefore opt to have something called a 'thoe' created by transplanting their big toe onto their hand. This may sound unusual, but the thoe improves the range of movements the hand can achieve without being a massive loss to the foot it was removed from.

An even more impressive application of using self-cells to help avoid rejection comes from a rather more intimate area. In 2014, doctors from Mexico and the US operated on four young women affected by Mayer-Rokitansky-Küster-Hauser Syndrome (MRKHS). This rare syndrome causes girls to be born with a completely or partially absent vagina.

The surgeons in this case took cell samples from each patient and then grew these cells on a bespoke biodegradable scaffold. After an average of 6.75 years of follow up, all four young women were happy with their transplants, and none were rejected by their immune systems.

DEFENCELESS

When we consider things like transplant rejection, the immune system can seem more like a foe than a friend. However, the tale of David Vetter, a boy without a functioning immune system, is a stark reminder of just how dependent we are on our natural defences.

David was in this world for just 20 seconds before he was transferred to a sterile bubble, where he spent the rest of his life in order to protect him from the microbes in the environment that would have killed him within days. Sadly, he died at the age of just 12 when a failed bone marrow transplant gave him an infection. He never got to drink Coca Cola, one of his life aspirations, and the closest he got to playing in the garden depended on a $50,000 (£36,700) NASA engineered suit, which he was only able to use six times before outgrowing it.

As David's story tragically reminds us, our defences are absolutely essential to keeping us alive. It is thanks to our immune systems that we are not just alive but thrive in this dirty, beautiful, bug-filled world.

HOW DOES THE BODY'S IMMUNE SYSTEM ADAPT?

A HIGHLY TARGETED DEFENCE FORCE PATROLS OUR BODIES THAT NOT ONLY DESTROYS PATHOGENS BUT ALSO REMEMBERS THEM FOR THE FUTURE

The innate immune system is the first line of defence against pathogens. It provides rapid protection, trapping foreign invaders, coating them in toxic chemicals, engulfing them and digesting their remains. Though highly effective, its protection is not tailored to specific invaders, and it has no way to remember what it has fought before.

This is where the adaptive, or acquired, immune system comes in. Every pathogen is covered in signature patterns (antigens) that can be exploited by the immune system to launch a targeted attack. T-cells and B-cells – i.e. lymphocytes – are able to recognise antigens using receptors on their cell surface. Random shuffling of genetic material generates unique antigen-detecting receptors in every cell, allowing each of the millions of lymphocytes to recognise a unique antigen. This means that whatever infection the body faces, there should always be a lymphocyte that can respond.

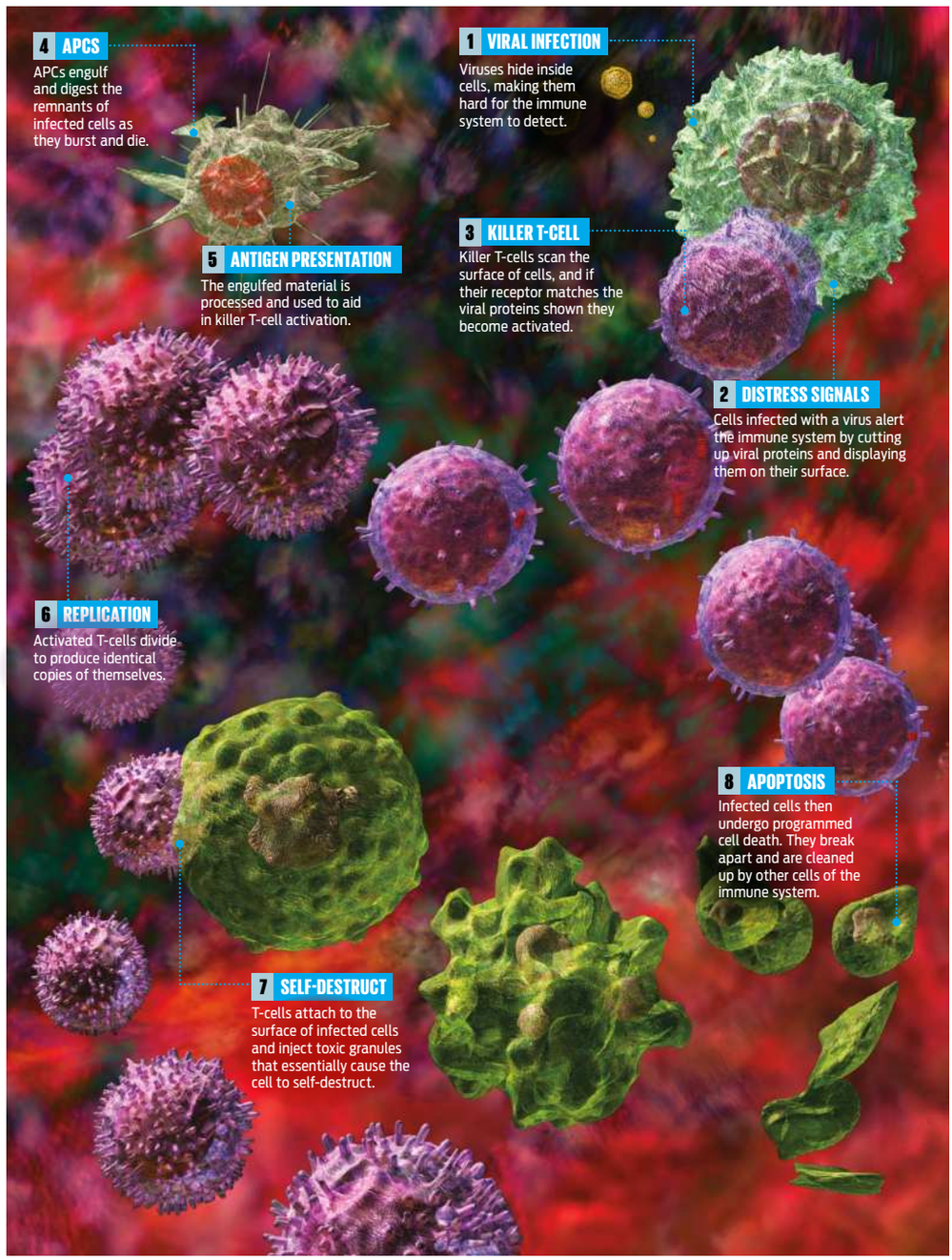
B-cells recognise antigens directly on the surface of pathogens, but T-cell targets often hide within human cells out of sight. Antigen-presenting cells (APCs) cut pathogens into fragments, which they then display for T-cells to examine. They also produce a cocktail of signalling molecules describing the location of the infection and the type of response needed.

Each person has millions of lymphocytes, so for any one pathogen there may only be a handful of cells with receptors that match the specific antigens. In order to make an army large enough to take down the invader, lymphocytes activated by their antigen divide rapidly to generate thousands more cells. This takes up to a week, during which time the innate immune system holds down the fort, keeping the infection at a manageable level.

While lymphocytes are dividing they also make 'memory' cells specific to the pathogen that remain in circulation for many years. If the pathogen returns, these reactivate and start to divide, often reacting so quickly that the pathogen is killed before it can cause illness.

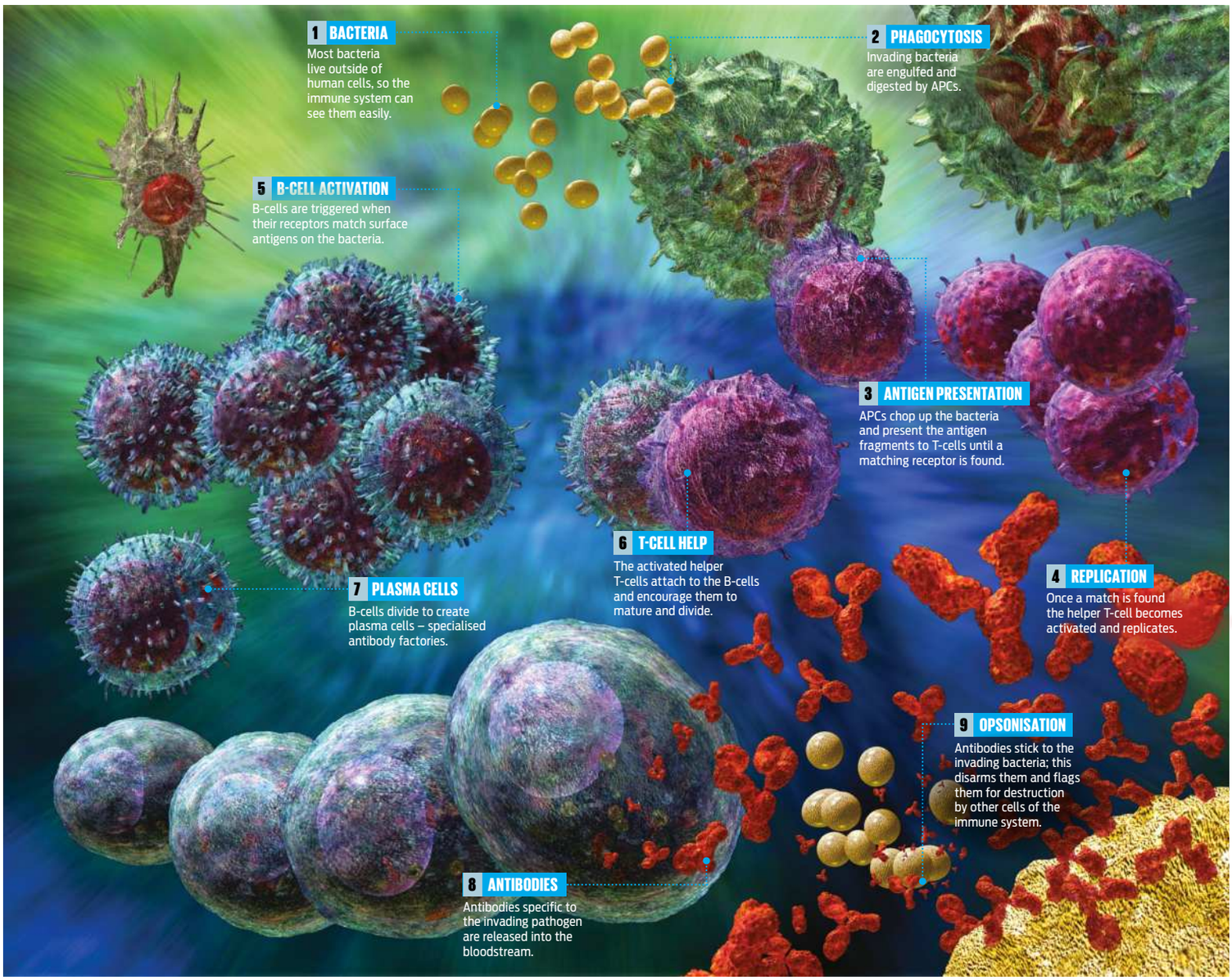
VANQUISHING VIRUSES

INFECTED CELLS ARE PROGRAMMED TO SELF-DESTRUCT TO TAKE OUT VIRUSES HIDING WITHIN



BATTLING BACTERIA

ANTIBODIES ARE THE MAIN DEFENCE AGAINST PATHOGENS THAT LIVE OUTSIDE HUMAN CELLS



VACCINATION AND IMMUNOLOGICAL MEMORY

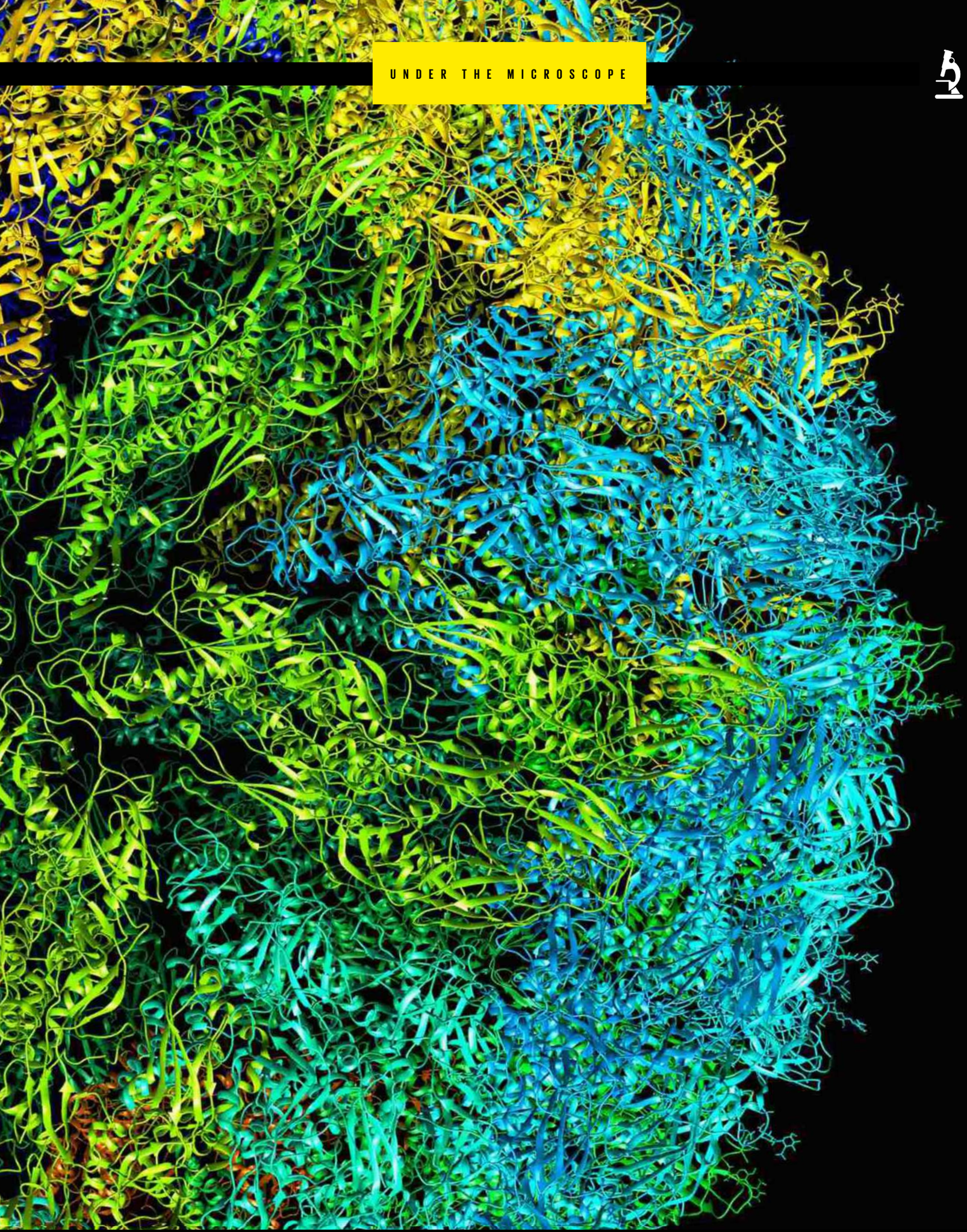
Immunity can be induced artificially through vaccination. Vaccines contain dead or deactivated bacteria and viruses; these don't cause disease but still trigger the adaptive immune response, generating memory cells. If the live pathogen is encountered in the future, the memory cells will rapidly divide and the acquired immune system will be able to respond immediately, preventing illness.

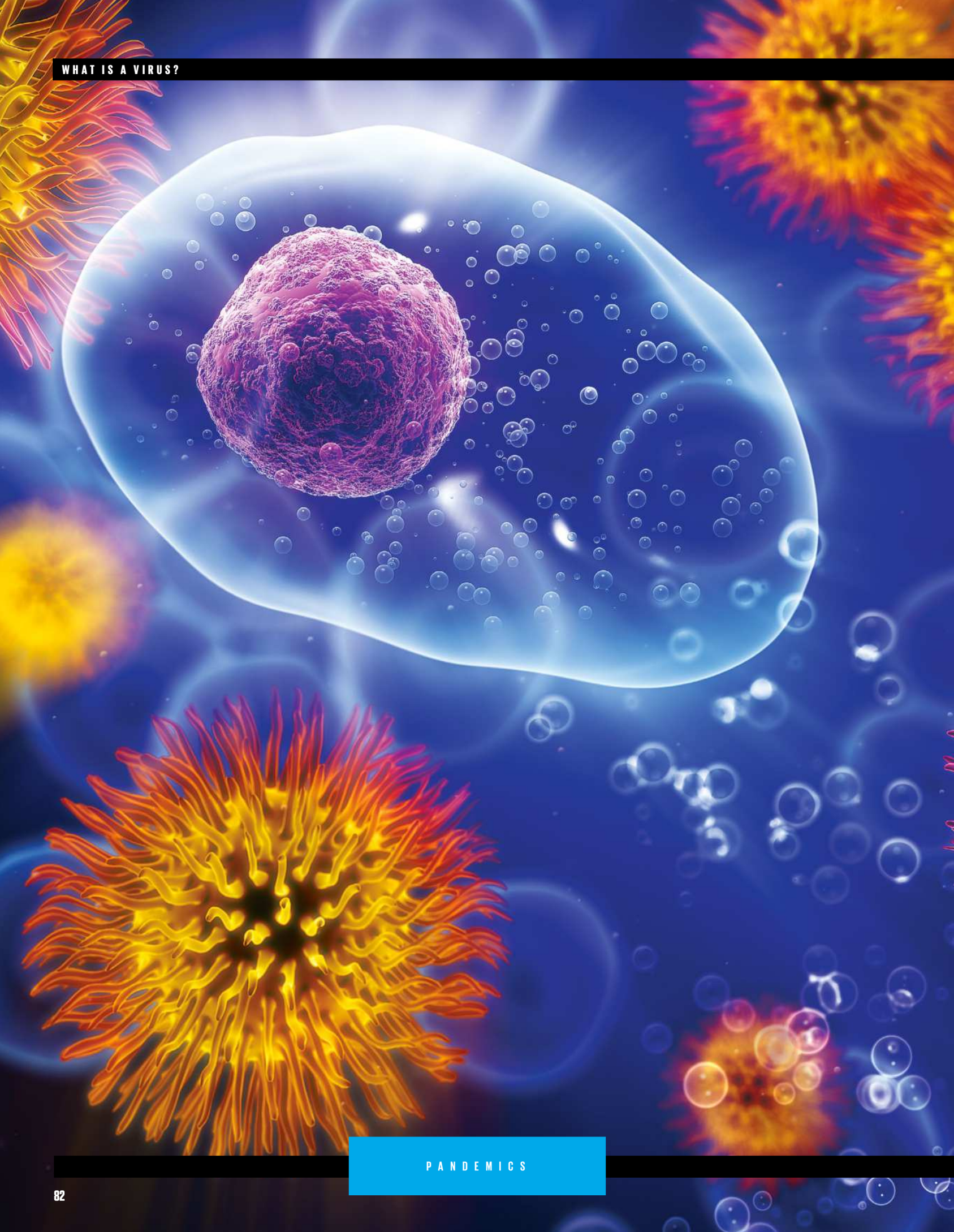
ZIKA

Named after the Zika Forest in Uganda, where it was first isolated in 1947, the Zika virus is spread by mosquitoes. Usually those who become infected don't display any symptoms, but occasionally patients will develop a rash or suffer from aching muscles, a high temperature or a headache. However, in the case of pregnant women, the situation can become serious.

Should an expectant mother become infected, the virus can pass to her fetus, which can result in birth defects including microcephaly, where a baby's head doesn't develop properly, resulting in a smaller skull and an underdeveloped brain. Scarring to the back of the eyes, reduced joint motion and excessive muscle tone, which can impact movement, are other side-effects of the virus in infants.

As a result of these risks, pregnant women are advised to avoid travelling to areas where the virus is known to be present. During an outbreak in 2015-2016 in the Americas, some governments went further, advising their citizens to delay pregnancy until more was understood about the long-term effects of Zika.





WHAT IS A VIRUS?

THESE TINY PACKETS OF GENETIC CODE ARE THE MOST SUCCESSFUL PARASITES IN THE WORLD

Viruses are the tiniest biological replicators on the planet, roughly 100-times smaller than bacteria. Made from a small strand of genetic code and covered with a tiny protein shell, they can't 'live' on their own. In fact, scientists aren't sure whether they're even alive at all.

The cells of living organisms have their own molecular production lines. They make temporary copies of their genes and pump them through molecular machines called ribosomes. These read the genetic code and use it as a template to assemble proteins. The simplest living organisms need between 150 and 300 genes to make all the proteins they need to survive, but viruses get by on as few as four. They simply hijack other cells and turn them into virus factories.

Viruses are clever; they make up for their genetic shortfall by borrowing from the cells they infect. Viruses don't have their own ribosomes, so they feed their code into the machines of other organisms, taking over the production line. The infected cell stops making its own proteins and starts reading virus code and assembling virus proteins.

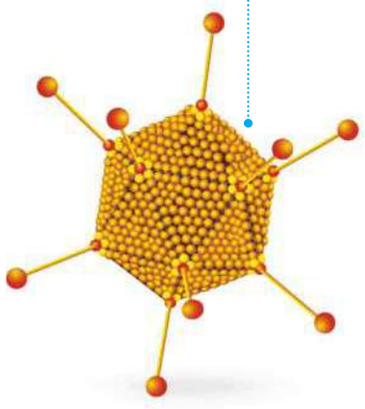
The core of a virus is its genetic code, which is stored in the same strings of biological letters used by living organisms. Some viruses have two strands of DNA like us, others get by with just one strand, and some carry their genes as RNA. This molecule is like DNA but with a different chemical letter, and it's used by living cells to make temporary copies of genes. Some viruses also carry the code to make an enzyme called reverse transcriptase, which allows them to convert RNA into DNA inside a living cell.

Genetic information is fragile, so to move from one cell to the next viruses need a way to protect their code. Some of their most important genes provide the instructions to build proteins that make a protective coat called a capsid. The capsid proteins form repeating structures that lock together to

Virologists use protective equipment to study human viruses in the lab

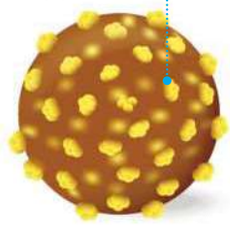
ALL SHAPES AND SIZES

VIRUSES MAY BE SMALL AND SIMPLE, BUT THEY'RE VERY EFFECTIVE



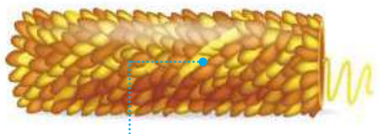
POLYHEDRAL

The outside of these viruses is a regular 3D structure, most often a 20-sided ball.



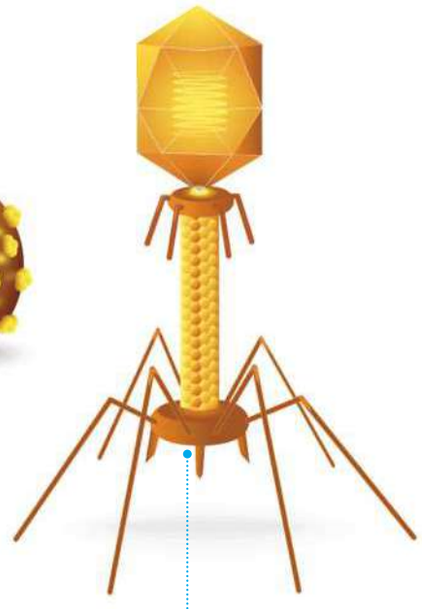
SPHERICAL

These viruses borrow membrane from the cells they infect, covering themselves in a fatty sphere.



HELICAL

The genetic code of these viruses is covered in a twisted tube-shaped coat.



COMPLEX

These viruses have irregular shapes and do not fit neatly into the other categories.

ARE VIRUSES ALIVE?

THIS IS STILL A TOPIC OF DEBATE AMONG SCIENTISTS. VIRUSES DO NOT FIT INTO OUR DEFINITIONS OF LIFE, BUT THEY SHARE SOME 'LIFE-LIKE' CHARACTERISTICS

ALIVE

"Viruses use the same molecular building blocks as other living organisms: RNA, DNA and protein"

"Viruses evolve and have made complex changes to their genetics to adapt to their unique environments"

"Lots of other parasitic organisms depend on others for survival and cannot exist on their own"

DEAD

"Viruses have a protective protein coat, but they do not have a membrane and are not cells"

"Viruses don't use any energy when they're floating between cells. They simply exist"

"Viruses cannot copy their own genetic code – they need living cells to do it for them"

make a 3D shape. This crystal-like patterning means that viruses only need a few genes to make a complete shield. Icosahedral capsids, for example, often contain small triangles made from just three proteins. These triangles slot together to make a 20-sided ball that covers the viral genome.

The infectious packages of capsid and genetic code can survive outside of cells, but they can't replicate on their own. Known as virions, these virus particles need to get back into cells to continue their lifecycle. They do this by attaching to molecules on the cell surface.

Proteins on the outside of the capsid interact with proteins on the outside of the cell. This attachment may change the shape of the virion itself, allowing the particle to fuse with the cell membrane. Alternatively, it might trick the cell into pulling the virus into a membrane-covered sphere known as an endosome. Once inside, enzymes carried by the virion – or from the cell itself – break down what's left of the capsid, releasing the genetic code into the cell. The viral genome then enters the cell's production line and quickly begins manufacturing three main types of protein.

The first are enzymes that enable the virus to construct more copies of its own genes. The second are proteins that interfere with the cell's normal manufacturing processes. The third type are the structural proteins that work to build new virus particles.

When the new virus particles are complete, the virus needs a way to release them to infect more cells. 'Lytic' viruses simply burst out, releasing all their virions in one huge pop and killing the cell in the process. 'Lysogenic' viruses release new virions one by one, allowing the host cell to survive and reproduce. Some viruses even stitch their genetic code into the code of their host, so that every time the cell divides the new cells also get a copy of the viral genes. This allows viruses to remain inside cells for a long time, staying dormant and then reactivating later, a property known as latency.

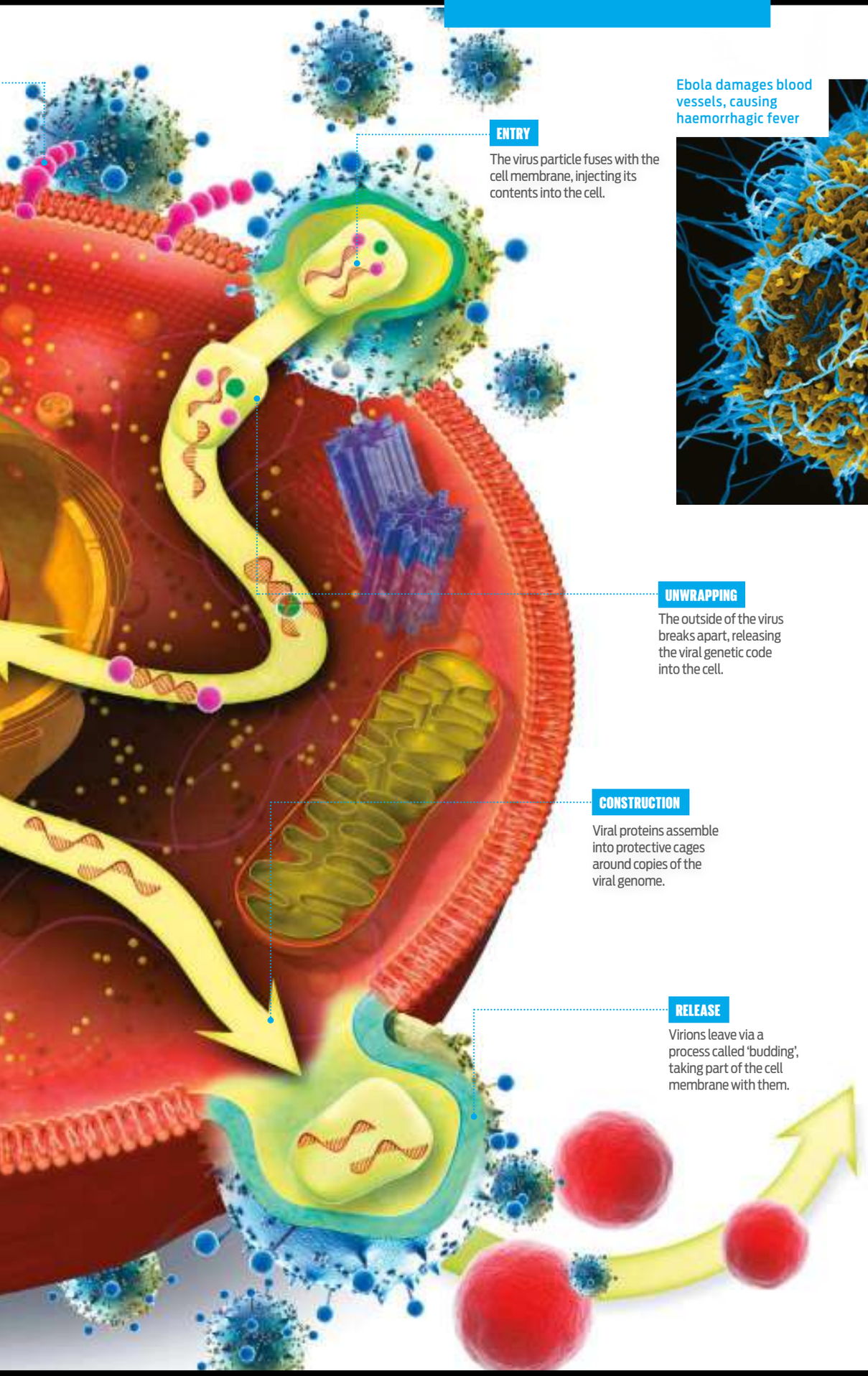
Cells do attempt to defend themselves from this type of attack. They destroy loose genetic code and send signals to the immune system to let it know about the infection. But viruses have evolved ways to evade these defences. In the process, some have gained characteristics that

"LYTIC VIRUSES SIMPLY BURST OUT, RELEASING ALL THEIR VIRIONS IN ONE HUGE POP"

VIRUS PRODUCTION

THESE PATHOGENS TURN CELLS INTO MINIATURE VIRUS FACTORIES

Below: the structure of an influenza virion



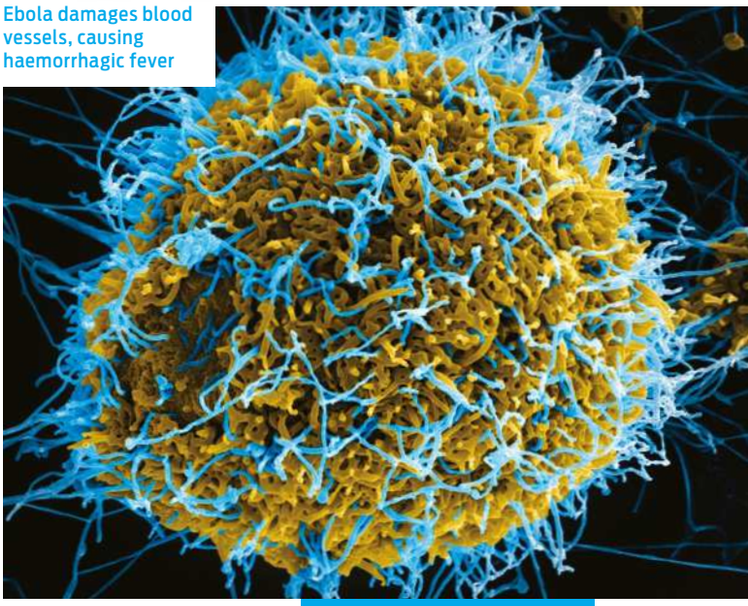
ENTRY
The virus particle fuses with the cell membrane, injecting its contents into the cell.

UNWRAPPING
The outside of the virus breaks apart, releasing the viral genetic code into the cell.

CONSTRUCTION
Viral proteins assemble into protective cages around copies of the viral genome.

RELEASE
Virions leave via a process called 'budding', taking part of the cell membrane with them.

Ebola damages blood vessels, causing haemorrhagic fever



5 DEADLIEST VIRUSES

1. Ebola
Ebola causes haemorrhagic fever, killing an average of 50 per cent of people infected. The outbreak between 2014 and 2016 in Africa was the largest ever recorded.

2. Marburg
Carried by fruit bats, Marburg virus is fatal in around 50 per cent of cases. It's part of the same virus family as Ebola, both of which damage the blood vessels.

3. Crimean-Congo haemorrhagic fever
This virus kills up to 40 per cent of people infected, usually within two weeks. It's transmitted by ticks in Africa, the Middle East and Asia.

4. Coronaviruses
MERS and SARS are types of coronaviruses that cause a cough, fever and breathlessness. MERS kills up to 35 per cent of patients.

5. Nipah
Nipah virus first appeared in 1998. It's carried by fruit bats and causes fever, headaches, drowsiness and sometimes fatal brain swelling.

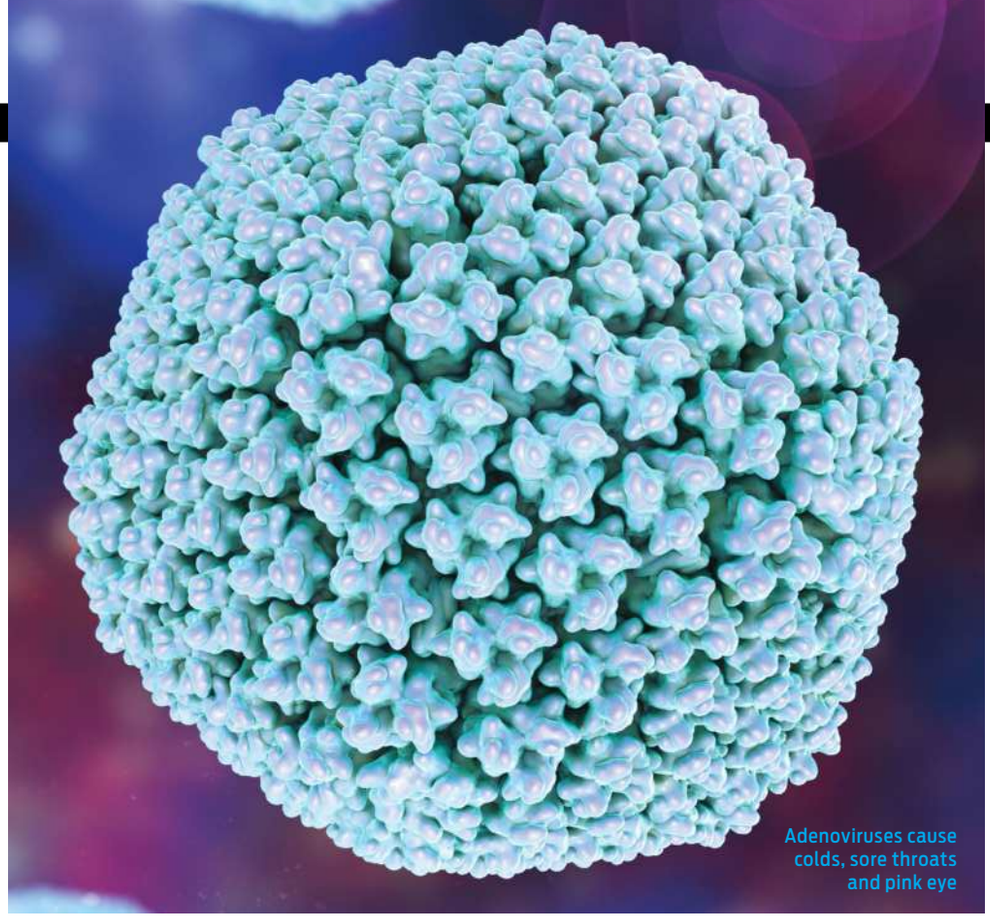
harm their hosts, a potentially lethal property that is known as virulence.

Many viruses cause disease, diverting healthy cells away from their normal activities. The type of damage a virus does depends on the cells it infects, the way it interferes with molecular machines and the way it releases new virions. Some of the most serious problems arise when viruses infect immune cells, preventing the body from fighting back. Ebola, Marburg and HIV all harm the immune system.

However, viruses aren't all bad; infections help to shape the way our bodies work. Studies of the human genome have revealed that around eight per cent of our genetic code actually came from viruses. Known as 'human endogenous retroviruses', or HERVs, they are easy to spot because they still carry the remnants of three viral genes: gag, pol and env. These genes belong to retroviruses, which stitch their genetic code into the genome of their host.

Retroviruses leave a permanent mark on DNA, and the results of ancient infections have been passed from parent to child for thousands of years. Evolution has gradually changed the sequence of these leftover viral genes, making them unable to produce new virions. Our bodies have found new uses for the code left behind.

One HERV, HERV-W, codes for proteins that would once have sat in the outer envelope of a virus, helping it to fuse with cells. We have adapted the code to make new proteins that help to fuse cell membranes together to form the placenta. Without the leftovers of ancient viral infections we wouldn't be here today.



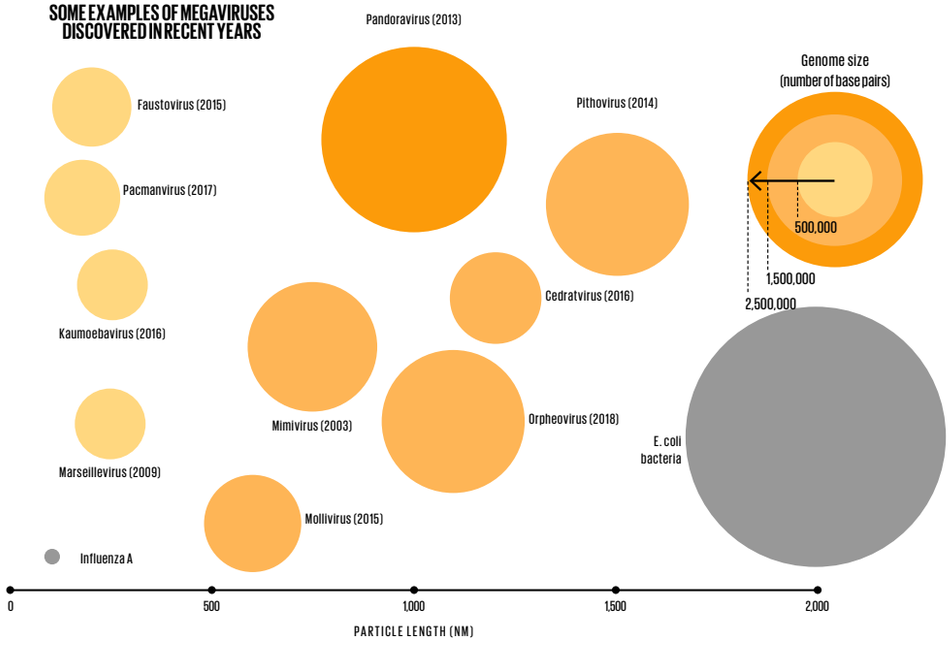
Adenoviruses cause colds, sore throats and pink eye

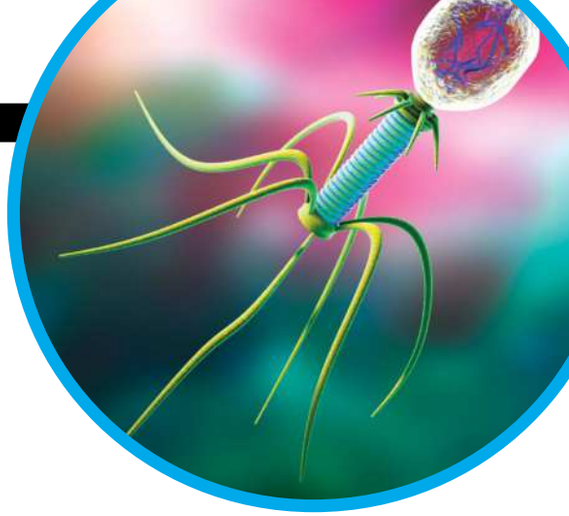
Bacteriophages inject their genetic code into bacteria cells, turning them into virus factories

THE GIANTS OF THE VIRUS WORLD

Viruses tend to have tiny genomes with only around 3,000 genetic letters. That's compared to around 3 billion in our own genome. They strip their genetics back to the bare essentials and borrow everything else from the cells they infect. Even so, there are a few unusual 'megaviruses' that buck the trend.

Mimivirus has a bloated genetic code containing 1.2 million letters. It's so enormous that when researchers first saw it they thought it was a bacterium. Unlike most viruses, it carries genes for building proteins, suggesting that it may have evolved from an organism that could once fend for itself. An alternative hypothesis is that it stole the genes from the cells it infected.





VIRAL VECTORS

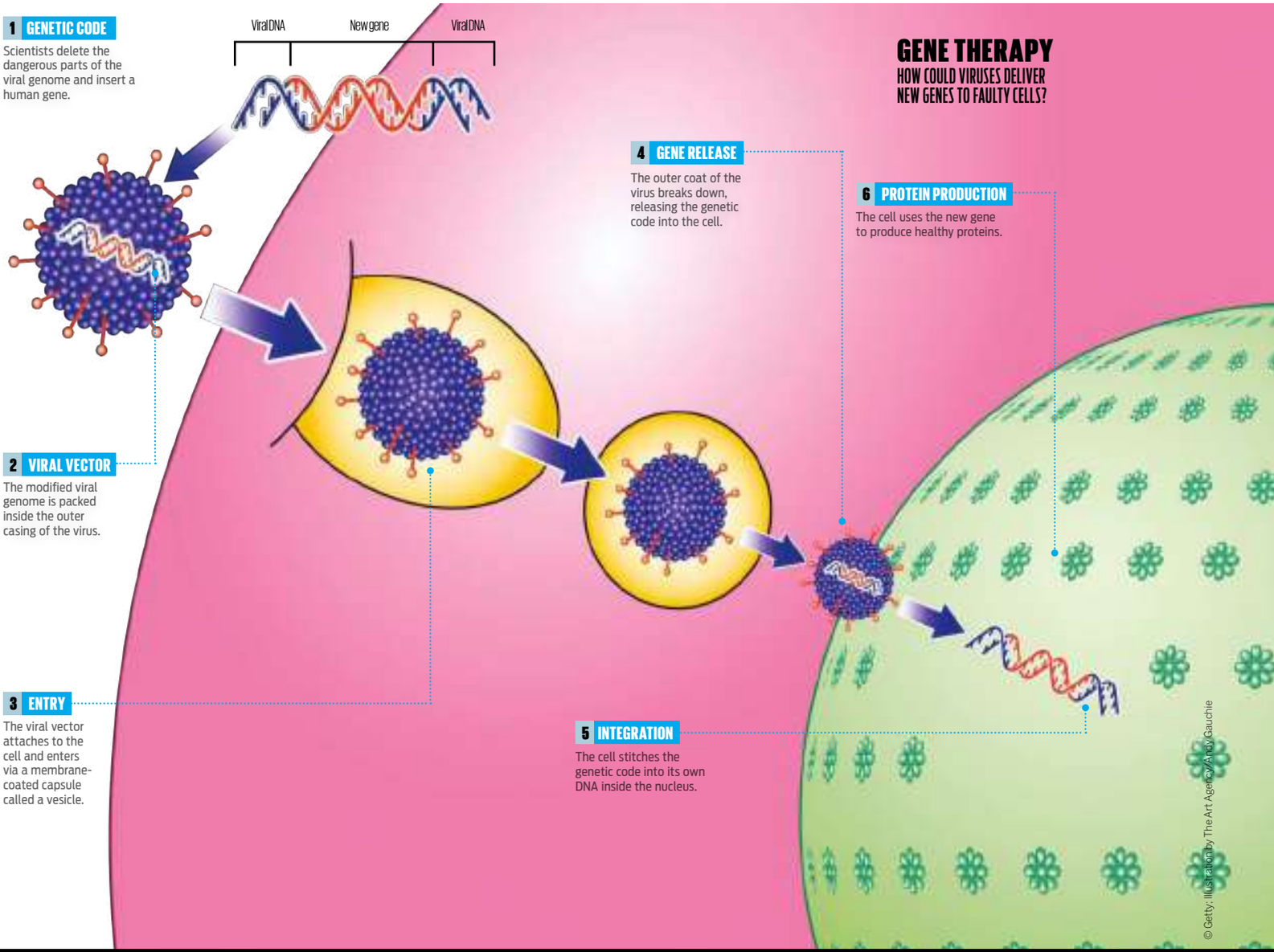
COULD SCIENTISTS TAME VIRUSES AND USE THEM TO SAVE LIVES?

Viruses specialise in getting past cellular defences to deliver genetic information into cells, but in nature they often contain genes that cause disease. However, if we strip out these damaging stretches of code we could use the outer virus packaging as a way to deliver useful genes to damaged cells. This is the idea behind viral vectors.

The first step requires scientists to delete the parts of the viral genome that allow viruses to make copies of themselves. Then they add the code for different genes. When the modified virus infects a cell it carries these new genes with it.

The most commonly used viruses for vector science are adenoviruses and retroviruses. Adenoviruses have a DNA-based genome and temporarily infect mammalian cells. The cells make viral proteins for a while and then revert to normal. Retroviruses are RNA-based and insert their genetic code into the genome of the cells they infect. This permanently changes the DNA of the cell, making it produce viral proteins forever.

In the lab, viral vectors allow scientists to find out what happens when cells gain the ability to make different proteins. Outside of the lab, viral vectors have the potential to fix broken genes by delivering fresh genetic code to human cells. However, the technology may be dangerous because it's hard to control exactly where the cell puts the new genes. Research is ongoing to find out if we can safely use viruses for gene therapy. If so, this process could totally revolutionise medicine and potentially save countless lives.



BACTERIA VS VIRUS

WHICH IS WHICH, AND WHY DOES IT EVEN MATTER?

When you've got a sore throat, the cause doesn't always seem important. Some microscopic nasty is waging war with your immune system, it hurts, and you just want to feel better. But whether it's bacteria or a virus on the rampage is actually very important.

Bacteria are some of the smallest living things on the planet, each made from just a single, primitive cell. Their insides are separated from the outside by a fatty membrane and a flexible coat of armour called a cell wall. Their genetic information is carried on loops of DNA, and these contain tiny factories called ribosomes, which use the genetic code to produce the molecules that the bacteria need to grow, divide and thereby survive.

Viruses, on the other hand, are not technically alive. They carry genetic information containing the instructions to build more virus particles, but they don't have the equipment to make molecules themselves. To reproduce, they need to get inside a living cell and hijack its machinery, turning it into a virus factory.

Both bacteria and viruses can cause diseases, but knowing which is the culprit is critical to treating them effectively. Antibiotics can harm bacteria but have no effect on viruses. Even your own immune system uses different tactics.

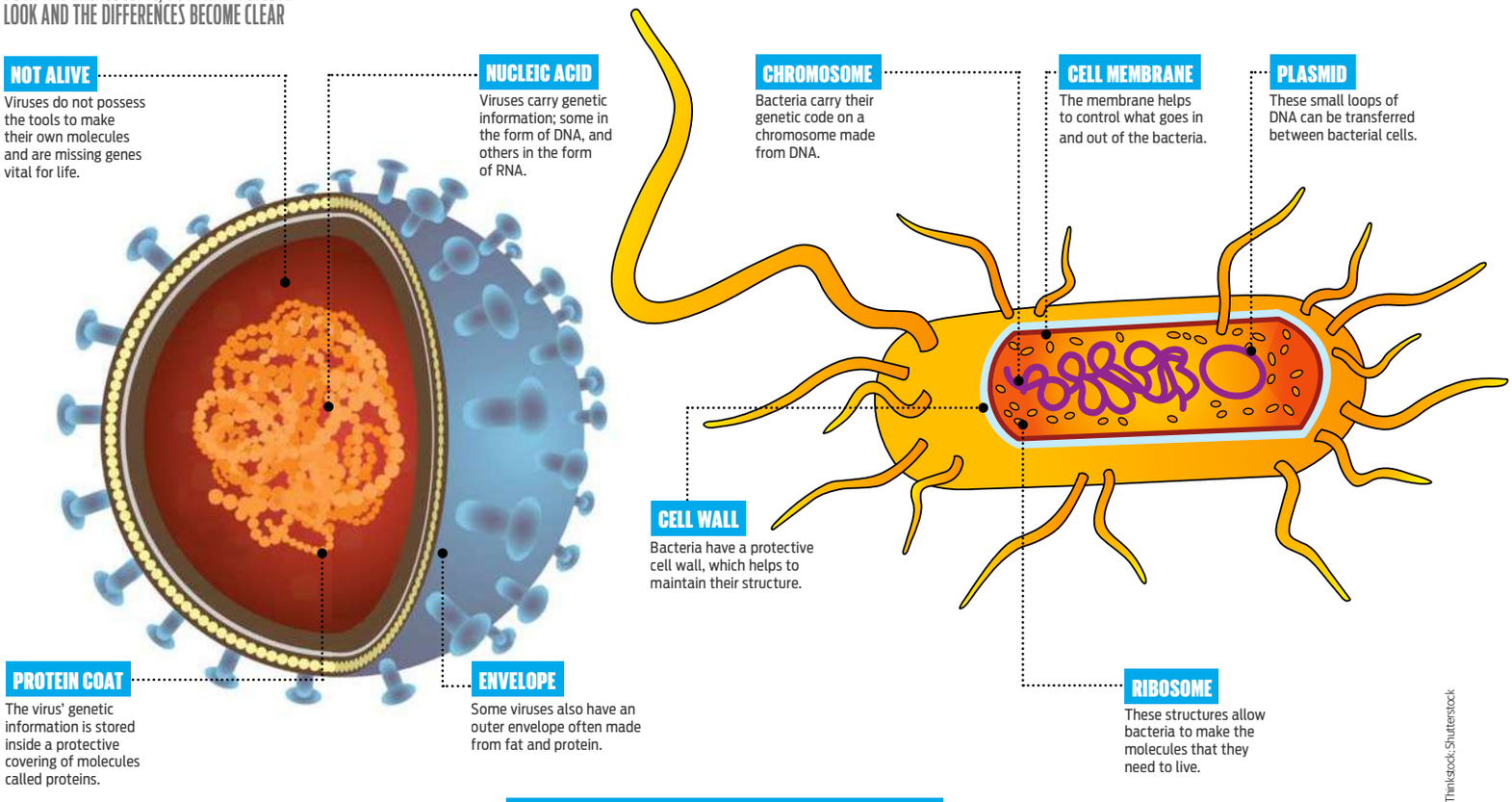
For bacteria, it unleashes antibodies – projectile weapons that stick invading microbes together, slowing them down and marking them for destruction. For viruses, your immune system can search for any infected cells before initiating a self-destruct sequence to dispose of anything lurking inside. But some viruses are able to endure our defences and can remain inside us indefinitely.

HEAD TO HEAD

Antibiotics attack bacteria. They work by interrupting the way that the tiny cells divide, grow and repair. However, if an infection is caused by a virus, antibiotics won't help. Viruses don't work in the same way as bacteria, so antibiotics can't help to fend them off. It might not seem like much of a problem, but every time antibiotics are used, it gives bacteria a chance to learn how to resist them. So every time a patient with a virus is given antibiotics, not only will they not get better, but bacteria lurking in their bodies will have a chance to see the drug and develop defences against it.

HEAD TO HEAD

BOTH ARE MICROSCOPIC, BUT TAKE A CLOSER LOOK AND THE DIFFERENCES BECOME CLEAR



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EBOLA VIRUS

DISCOVER HOW THIS DEADLY VIRUS ATTACKS THE BODY AND SPREADS BETWEEN HUMANS

When it comes to lethal viruses, Ebola has few equals. With the ability to kill up to 90 per cent of those it infects, Ebola is a devastating biological weapon. An outbreak in 2014 in West Africa caused over 11,000 deaths across Guinea, Liberia and Sierra Leone, leaving many people confused and scared about this infectious and often fatal disease.

Ebola virus disease (EVD) is spread via contact with the blood, bodily fluids and organs of an infected person or animal. A person only becomes infectious once their symptoms start to show, which is usually two to 21 days after infection. The initial symptoms are a sudden onset of fever, fatigue, muscle pain, headache and sore throat, followed by vomiting, diarrhoea and rashes, eventually leading to impaired kidney and liver function, as well as internal and external bleeding.

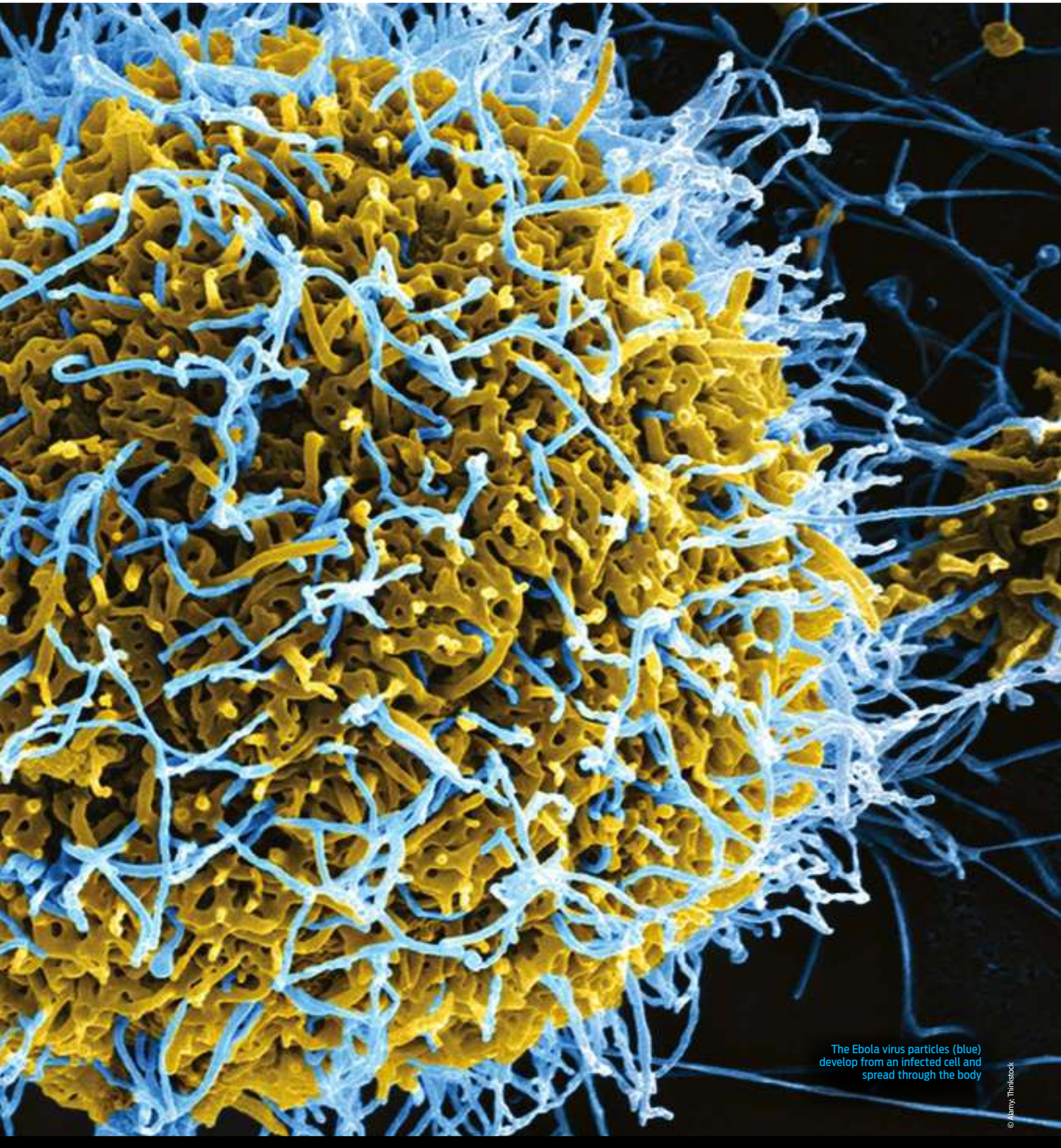
There have been many outbreaks since the disease first appeared in 1976, but the most recent has the highest death toll due to it spreading to urban areas instead of being contained in rural villages.

There is currently no licensed treatment for Ebola, but there are potential vaccines currently being developed and tested. However, the chances of survival are significantly improved if the body is quickly rehydrated, buying time for it to fight off infection.

The shape and structure of the Ebola virus makes it a particularly virulent one

WHY IS EBOLA SO DEADLY?

Instead of being sphere-shaped, like most viruses, the Ebola virus is actually long and thin, giving it a larger surface area for attacking a larger number of cells. The virus is also covered in attachment proteins that bind to the receptor sites of human cells and release the virus' genetic material, allowing it to take over healthy human cells and replicate itself into new copies of the virus. Once it enters the body, it will first aim to disarm the immune system so that the white blood cells can't fight off the virus before it spreads quickly. As a haemorrhagic fever virus, the infected cells release proteins that cause blood to leak out of the vessels. This is what causes the most extreme and often fatal symptoms of Ebola: impaired kidney and liver function, a drop in blood pressure and internal and external bleeding.



The Ebola virus particles (blue) develop from an infected cell and spread through the body

THE RISE OF SUPERBUGS

HOW THE WIDESPREAD OVERUSE OF ANTIBIOTICS IS PROVING THAT TOO MUCH OF A GOOD THING CAN BE CATASTROPHIC

Antibiotics are without question the miracle drugs of the 20th century. Penicillin, the first widely produced antibiotic, saved more soldiers' lives during World War II than the Sherman tank. Since the 1940s researchers have discovered newer, more powerful strains of antibiotics to treat everything from a common ear infection to the most exotic tropical disease.

When a young mother or father takes their sick child to the doctor complaining of high fevers, green mucus and listlessness, they don't want to hear the standard speech about drinking lots of liquids and getting plenty of rest - they want something that will alleviate the symptoms almost instantly. They want to be given antibiotics. Sadly, many doctors are more than happy to prescribe them, whether patients really need them or not.

According to the United States Centers for Disease Control, antibiotics are wrongfully administered in almost 50 per cent of cases. On an individual level there's no real harm in unnecessarily taking an antibiotic. However, widespread abuse of antibiotics has a potentially catastrophic effect on society as a whole. The more antibiotics that humans - and the animals we eat - take, the quicker bacteria evolve and the stronger they become. And what happens when bacteria evolve so significantly that our beloved antibiotics no longer have any effect on them? The answer is a potential health crises.

Antibiotic resistance is one of the world's most serious health threats. We are already witnessing the rise of so-called 'superbugs', pathogenic bacteria that are immune to traditional antibiotic treatment. One of the best known superbugs is MRSA, short for methicillin-resistant Staphylococcus aureus.

Like several other drug-resistant bugs, MRSA spreads quickly through hospitals on the unwashed hands of health workers and patients.

Pre-surgery antibiotics can prevent infection

Staph infections are nasty enough. If allowed to enter the body they can target the lungs (pneumonia), the heart (endocarditis) and even the bloodstream (bacteraemia). MRSA is staph on steroids, because it has evolved to be resistant to the most effective antibiotics for curing the infection. Imagine going into the hospital with a sprained ankle and leaving with a drug-resistant case of pneumonia.

So how do common bacteria like S. aureus and E. coli evolve so quickly from a curable annoyance to a potential pandemic? Let's start by dusting off our Darwin. Evolution by natural selection requires three things: reproduction, variety and selective pressure. Bacteria are masters of reproduction. Under the right conditions a bacterial colony will double in size every ten minutes. They do this through binary fission. Essentially the bacteria makes a copy of its own DNA, then splits in two. With so much copying and splitting, some mistakes - in the form of mutations - are going to be made. These genetic mutations increase the variety of traits that the bacteria can express. Variety is not only the spice of life but also the engine of evolution.

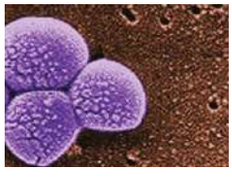
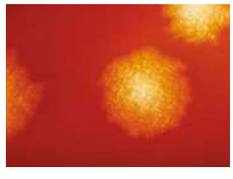
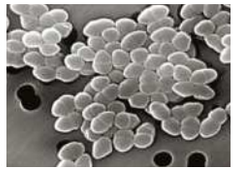
When a doctor administers an antibiotic to kill off an infection of S. aureus, this applies a selective pressure to the bacterial colony. Bacteria that express beneficial traits - such as the ability to pump antibiotics out of their system - will survive, while the others will be wiped out. The surviving bacteria will then repopulate the colony, and the next time the antibiotic is applied, it will be completely useless due to the bacteria's evolution.

Bacteria are not only evolutionarily efficient, they are also cheaters. Through a process called conjugation, two bacteria can share slices of genetic material that carry beneficial traits, skipping the randomness of natural selection altogether. By this method, some bacteria have developed techniques for disguising themselves to antibiotics, blocking the entrance to the cell wall and even tricking the body's own immune system to release toxic levels of proteins.

The best weapon against the spread of superbugs is to reduce our overall consumption of antibiotics - including in the beef, pork and dairy industries, which are responsible for administering approximately 80 per cent of the antibiotics in America - and to improve hygiene and sanitation at hospitals, where these infections thrive and spread. In this arms race, failure really is not an option.

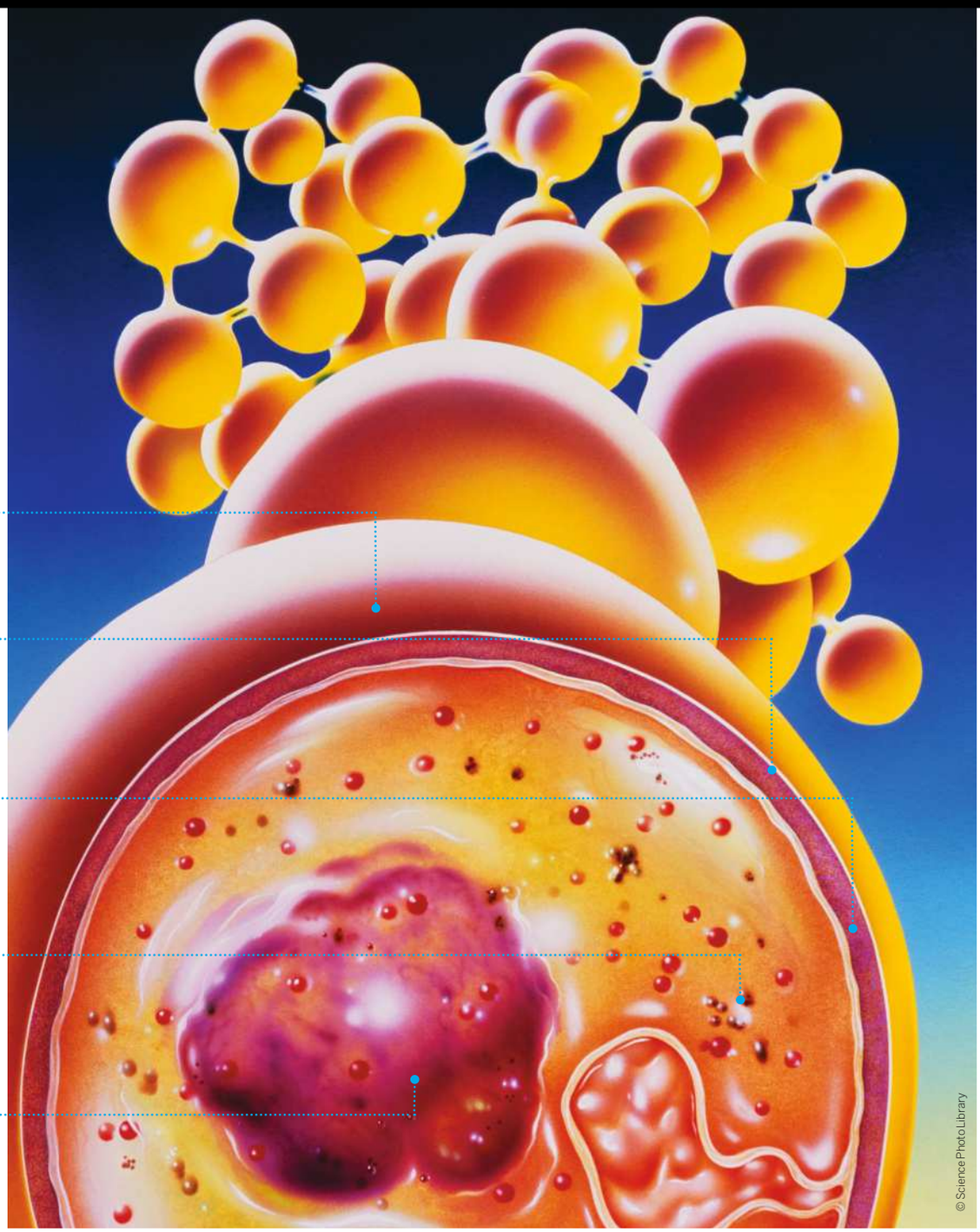
TYPES OF SUPERBUG

SUPERBUGS COME IN SEVERAL FLAVOURS, ALL MUTANT VARIATIONS OF RELATIVELY COMMON AND EVEN HARMLESS BACTERIA THAT NORMALLY LIVE IN OR ON THE HUMAN BODY. FUELLED BY THE OVERUSE OF ANTIBIOTICS, THESE NOVEL STRAINS NOW HAVE DEADLY POTENTIAL

METHICILLIN-RESISTANT *STAPHYLOCOCCUS AUREUS* (MRSA)	*SHIGA TOXIN-PRODUCING ESCHERICHIA COLI 0104:H4*	*DRUG-RESISTANT CLOSTRIDIUM DIFFICILE NAP1 (C. DIFF)*	*VANCOMYCIN-RESISTANT ENTEROCOCCI (VRE)*
YEAR DISCOVERED			
1960	EARLY 1990S	EARLY 2000S	1986
INFORMATION			
While staph infections are common and usually curable with standard antibiotics, MRSA is stubbornly resistant to a family of antibiotics called beta-lactams. Most MRSA cases start as skin infections around wound sites, often exhibiting pus-filled boils. Life-threatening cases can involve blood infections, surgical site infections and pneumonia.	E. coli is transmitted to humans through food or water contaminated with animal faeces. Most cases can be treated with antibiotics, but the deadly strain 0104:H4 is resistant to most major classes. In fact, antibiotic treatment triggers the release of toxins that make the symptoms – which include violent diarrhoea, kidney damage and blood clots – far worse.	Like MRSA, C. diff thrives in hospital settings and is resistant to many treatments. A C. diff infection is most often caused by prolonged antibiotic treatment. While antibiotics kill off unrelated infections, C. diff remains unharmed, colonising the gut and releasing a powerful toxin that causes colitis, severe diarrhoea and even perforation of the colon.	Enterococci bacteria live in the healthy human gut and female genital tract. But certain conditions can cause them to grow out of control, leading to urinary tract and even blood infections. The most powerful trigger is treatment with the antibiotic vancomycin. While this kills off harmful and healthy microbes, the Enterococci stay behind and thrive.
RESISTANT TO			
Methacillin, oxacillin, penicillin, amoxicillin.	Eight classes of antibiotics including beta-lactams (penicillins), tetracycline and cephalosporins.	C. diff infections emerge after treatments with penicillins, clindamycin, cephalosporins and fluoroquinolones.	Vancomycin.
RISK ENVIRONMENTS			
Shared spaces: hospitals, locker rooms, day care centres, university dorms, barracks and prisons.	Unwashed fresh fruits and vegetables pose the greatest risk of carrying the disease.	Hospitals. C. diff spores can live on contaminated surfaces for months.	Long-term hospital stays, especially with use of urinary catheters.
NUMBER OF DEATHS			
19,832 deaths in the US in 2017; 292 deaths in England and Wales in 2012.	53 deaths in the 2011 European outbreak.	Five per cent mortality rate within 14 days of sample collection.	In 2017, 54,500 patients in US hospitals were infected, causing 5,400 deaths.
TREATMENT			
Cleaning, incision and drainage of the wound. Testing to determine bacteria type and use of a targeted antibiotic.	Hydration, pain relief and close monitoring for severe symptoms like kidney failure or blood clots.	It can resolve itself a few days after antibiotic treatment ends. Others will need a stronger course of antibiotics like metronidazole.	Lab tests will indicate which antibiotics other than vancomycin can be used to treat the infection.
PREVENTION			
Avoid skin-to-skin contact with hospital patients or others with open wounds. Wash hands thoroughly after hospital visits, trips to the gym and so on.	Thoroughly wash fruits and vegetables and fully cook all meat and poultry products before eating.	Ensure hospital staff wash hands before touching you or your food. Transmission by healthcare workers is the number one transmission method for C. diff.	Better hospital sanitation, limited use of antibiotics and frequent changing of catheters.
			

INSIDE AN MRSA BACTERIUM

MRSA is a drug-resistant strain of *Staphylococcus aureus*, one of the most virulent and violent bacteria we know. Staph infections come in all flavours, from diarrhoea-inducing food poisoning to skin lesions to potentially fatal cases of toxic shock syndrome. MRSA is a staph bacterium that has mutated or otherwise acquired genetic traits that defend it against attacks from antibiotics.



1 CELL WALL

The outer surface of the bacterium is covered with proteins called adhesins that help the organism stick to damaged tissue surfaces.

2 ANTIGENS IN DISGUISE

The immune system produces antibodies that hunt down pathogenic bacteria like staph. The bacteria uses a surface protein called Protein A to bind antibodies to its surface and disguise itself as one of the good guys.

3 TOXIC COCKTAIL

Inside the cell wall, enzymes produce virulent varieties of leukotoxins and exotoxins that damage and destroy blood cells and living tissue, producing the lesions, boils and open sores that are symptoms of staph infections.

4 SUPER-ANTIGENS

The most severe staph infections are caused by enterotoxins and toxic shock syndrome toxins produced by intracellular enzymes. These so-called super-antigens trick the immune system's T cells into releasing huge amounts of a potentially deadly protein.

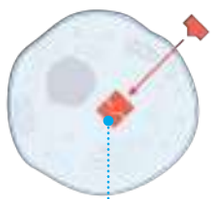
5 NUCLEOID

Antibiotics attack staph bacteria by targeting an enzyme that controls DNA replication inside the nucleoid. MRSA bacteria have mutated or acquired genes from other microorganisms that make them resistant to certain antibiotics.

"THROUGH DARWINIAN EVOLUTION, THE STRONGEST, MOST-RESISTANT BACTERIA SURVIVE AND SPREAD"

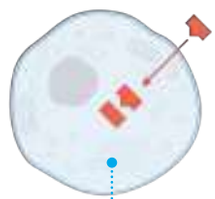
WHY ANTIBIOTICS DON'T WORK

Bacteria exist in our bodies by the billions. Some 1,000 different species live in the human gut alone. With such a large and thriving population, it's easy to understand how a few bacteria might randomly acquire traits that make them more resistant to 'killer' drugs like antibiotics. Through Darwinian evolution, the strongest, most-resistant bacteria survive and spread. Bacteria acquire these resistant traits through two mechanisms: genetic mutations or by genetic transfer from other organisms. These new traits effectively block antibiotic particles from reaching their target enzymes inside the bacterial cell wall.



1 TARGET SITE

In a normal bacterium the antibacterial treatment attaches to targeted bacterial enzymes, stopping DNA replication.

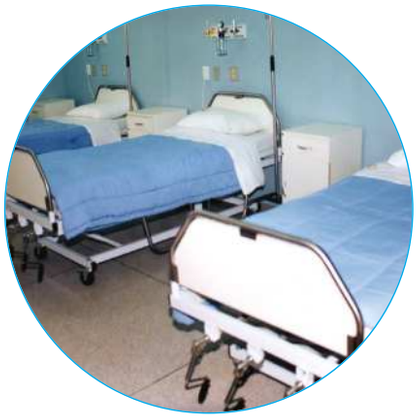


2 MUTATION

Random gene mutations cause the enzymes to change shape or chemical make-up, so the antibacterial agent can't attach.

SUPERBUGS AND HOSPITALS

For bacteria, a hospital is like an evolutionary experiment gone mad. Think about how many antibiotics are prescribed in a hospital, and think about the broad range of pathogenic bacteria that walk through the door on the skin and in the mouths, noses, ears and open wounds of patients. Even after we bomb these bacteria with drugs, a few hardy mutants will survive. These germs pass easily from patient to patient on unwashed hands and contaminated surfaces. A healthy patient might come in for a couple of stitches and leave with a raging, drug-resistant infection.



© Kurhan

HEALTHCARE WORKERS

Skin-to-skin contact is the most effective way to spread a superbug. Health workers must wash hands between patients and before leaving a patient's room.

ISOLATION AND COHORTS

Patients who are known to be MRSA positive should be isolated from the general population and special precautions should be taken by healthcare workers and visitors. Several MRSA patients can be bedded together as a cohort.

CATHETERS AND IVS

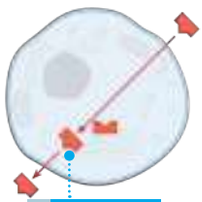
Health workers need to take particular care when inserting catheters or IVs. MRSA skin infections can easily pass into the urinary tract or bloodstream if proper hygienic precautions aren't taken.

SURFACE CONTAMINATION

Studies have shown that hospital surfaces like computer keyboards, tap handles, pens and doctors' scopes contain surprisingly high levels of pathogenic bacteria.

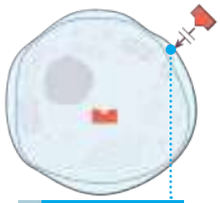
GLOVES AND SCRUBS

To further reduce the transmission of superbugs on skin and clothing, some hospitals require the use of disposable gloves and temporary clothing like scrubs in high-risk areas.



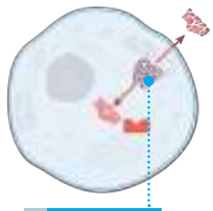
3 EFFLUX PUMP

Some bacteria have evolved a valve in the cell wall that can actively pump out antibacterial agents as they enter the cytoplasm.



4 SOLID CELL WALLS

Antibacterial agents enter via porin – tiny holes in the cell wall. Some mutated bacteria lack sufficient porin to allow a lethal amount in.



5 INACTIVATION

Some bacteria have evolved destructive enzymes that swim through the cytoplasm, zapping antibiotic agents before they can reach the target site.

5x© Science Photo Library

10 TIPS TO PREVENT THE SPREAD OF SUPERBUGS

1. Recognise that the overuse or misuse of antibiotics is a major cause of increasing antibiotic resistance.

2. Understand that antibiotics can only cure bacterial infections, not viral infections like colds or the flu.

3. Never take leftover antibiotics that you find in your house.

4. When prescribed antibiotics, follow your doctor's instructions and take the full course, which is usually the entire bottle.

5. Never take antibiotics prescribed to a friend just because you have the same symptoms as them.

6. Unless your symptoms are severe, take the time to have tests taken to determine the exact bacterial pathogen that's affecting you. This will allow your doctor to prescribe a targeted antibiotic instead of a wider-spectrum treatment.

7. Even if you and your doctor feel that you probably have an infection, ask about alternative treatments and remedies that might resolve the infection without the use of antibiotics.

8. Support farms and dairies that don't use prophylactic antibiotic treatments to stave off infections among their animals. Overuse of agricultural antibiotics is one of the greatest causes of antibiotic resistance.

9. Don't use low-level antibiotics to resolve chronic acne. Try other methods instead.

10. Healthcare professionals and hospital visitors must be vigilant about hand washing and overall sanitation, particularly when around patients who are immuno-compromised.

THE SMALLPOX VACCINE

ONE OF THE MOST TERRIBLE DISEASES TO HAVE EVER PLAGUED HUMANITY, SMALLPOX CLAIMED THE LIVES OF MILLIONS WORLDWIDE UNTIL IT WAS ERADICATED IN 1980

While our written records of the disastrous effects of the smallpox disease only extend back to the 15th century, there is compelling evidence that the disease emerged in human populations as far back as 10,000 years ago.

Indeed, upon close examination of the mummified remains of ancient Egyptian Pharaoh Ramesses V (who ruled c. 1150-1145 BCE), tell-tale pustular rashes can be seen, indicating that he most likely died from the disease. Since its emergence, both strains of the smallpox - variola major and variola minor - were left unchecked, leading to an estimated 400,000 Europeans dying each year throughout the 18th century.

In 1796, however, the game changed. English physician Edward Jenner realised that individuals who caught the cowpox virus (an incredibly mild and non-deadly variant of the vaccinia virus) did not catch smallpox. Jenner then proceeded to test the theory in a series of cases that even included his own son, infecting each with the cowpox and then smallpox viruses. None of the test cases became infected with smallpox and, as a direct consequence, the first successful vaccine in the world was created.

Here, we explore the science behind the smallpox virus, its vaccine and the history of its effects, as well as its eventual eradication.

SMALLPOX SYMPTOMS

The incubation period for smallpox is roughly 12 days. After this, those infected experience fever, muscle pain, headaches, nausea and backache. These symptoms are then followed by the disease's characteristic pimpled rash across the sufferer's skin, which emerges first on the forehead and then proceeds down the body. Finally, the disease transforms into one of four varieties: ordinary, modified, malignant and haemorrhagic – each of which varies in its overall fatality rate.

5 FACTS ABOUT EDWARD JENNER

1. APPRENTICE

Edward Jenner trained from the age of 14 for seven years in Chipping Sodbury, Gloucestershire, under surgeon Daniel Ludlow. In 1770, Jenner became apprenticed in St George's Hospital, Tooting, England.

2. CUCKOO

Jenner was elected Fellow of the Royal Society in 1788 following his publication of an in-depth study of the previously misunderstood life of the nested cuckoo. The report consisted of observations, experiments and dissections.

3. INSTITUTION

Off the back of his discovery and creation of the smallpox vaccine, Jenner became heavily involved with the Jennerian Institution in 1803, a society largely concerned with promoting vaccination and the eradication of smallpox.

4. KING

Due to his pioneering medical work, in 1821 Jenner was appointed physician extraordinary to King George IV, a great national honour. In the same year he was made mayor of Berkeley, his hometown.

5. STROKE

Edward Jenner died at the age of 73 from multiple strokes, the first leaving him paralysed and the second killing him. He was buried in the Jenner family vault at the Church of St Mary, Berkeley.

JOURNEY TO IMMUNISATION

DEVELOPING INOCULATIONS HAS BEEN A LONG, HARD ROAD, BUT THE DESTINATION WAS WORTH IT

68000-16000 BCE
The first smallpox virus evolves from a pre-existing rodent virus in Asia. One clade was the more deadly variola major strains, while the other clade included the less severe types of variola minor.

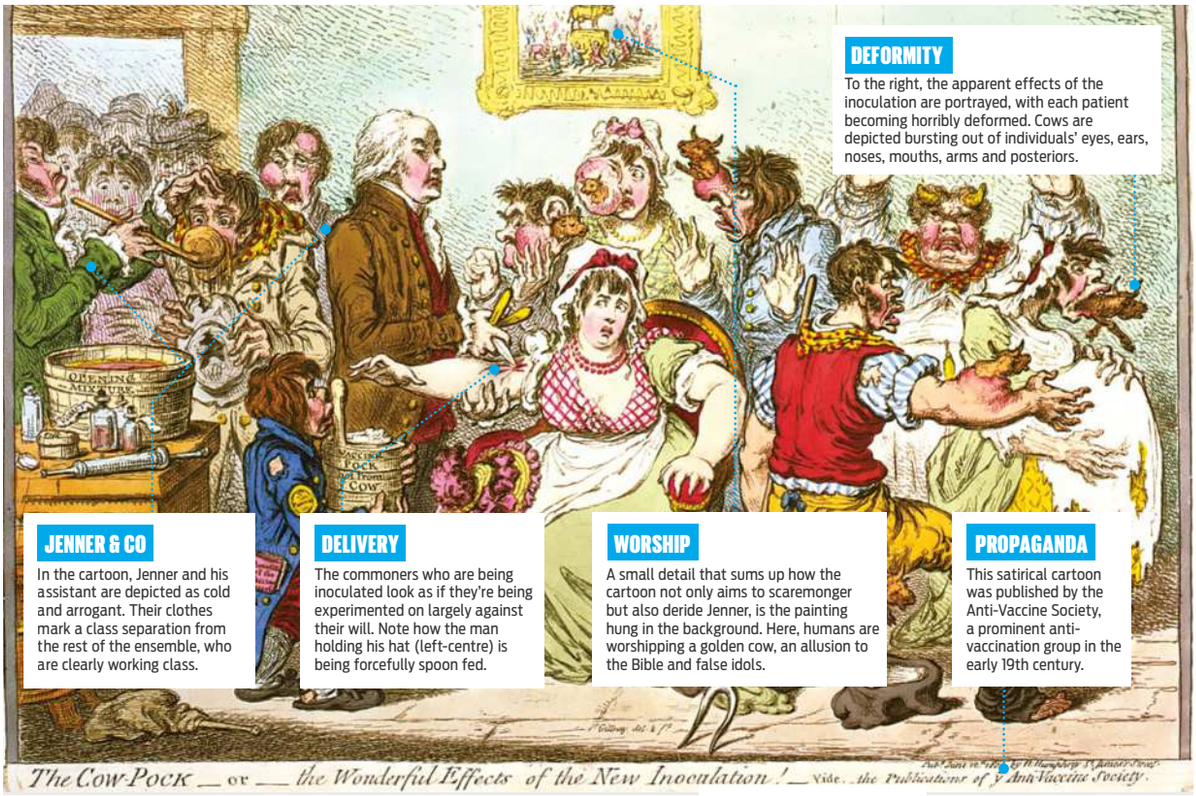
1500 BCE
The ancient Egyptians bring smallpox over to Egypt from India and China. The virus proceeds to take hold, claiming many lives including, most probably, that of Pharaoh Ramesses V.

700 CE
Arab armies carry the smallpox virus out of Africa and into Europe throughout the 7th and 8th centuries. The following Crusades continue this transference, leading to its widespread establishment in Europe.

1585
Book XII of the 16th-century *Florentine Codex* – an ethnographic research project carried out in Mesoamerica – details how the native Nahua people of Mexico suffer greatly from smallpox (right).

THE VACCINATION WAR

WHILE JENNER'S BREAKTHROUGH IS OBVIOUS FROM A MODERN PERSPECTIVE, THE IDEA OF INJECTING PEOPLE WITH ONE VIRUS TO PROTECT AGAINST ANOTHER CAUSED GREAT CONTROVERSY IN HIS TIME



DEFORMITY
To the right, the apparent effects of the inoculation are portrayed, with each patient becoming horribly deformed. Cows are depicted bursting out of individuals' eyes, ears, noses, mouths, arms and posteriors.

JENNER & CO
In the cartoon, Jenner and his assistant are depicted as cold and arrogant. Their clothes mark a class separation from the rest of the ensemble, who are clearly working class.

DELIVERY
The commoners who are being inoculated look as if they're being experimented on largely against their will. Note how the man holding his hat (left-centre) is being forcefully spoon fed.

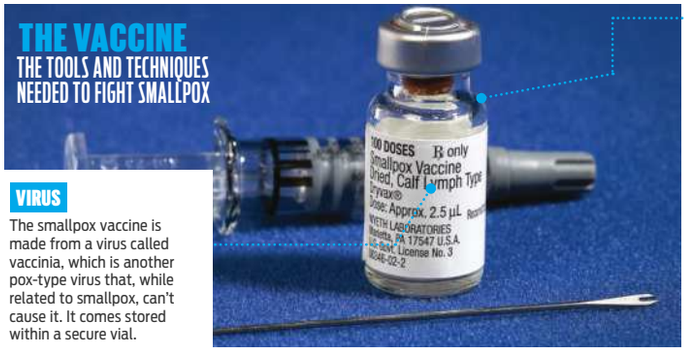
WORSHIP
A small detail that sums up how the cartoon not only aims to scaremonger but also deride Jenner, is the painting hung in the background. Here, humans are worshipping a golden cow, an allusion to the Bible and false idols.

PROPAGANDA
This satirical cartoon was published by the Anti-Vaccine Society, a prominent anti-vaccination group in the early 19th century.

BIRTHPLACE OF THE CURE TO SMALLPOX

Edward Jenner's house, the place where he undertook the most important work in his formulation of the vaccination against smallpox, still stands today. Located in the town of Berkeley, Gloucestershire, the house is now the Edward Jenner Museum, which combines a traditional museum with an interactive learning environment for children and a historical archive. For more information, readers can visit **www.jennermuseum.com**.

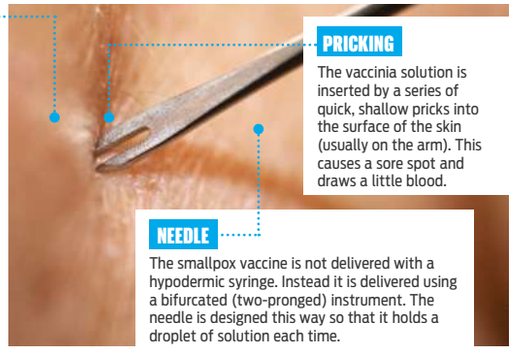
THE VACCINE
THE TOOLS AND TECHNIQUES NEEDED TO FIGHT SMALLPOX



VIRUS
The smallpox vaccine is made from a virus called vaccinia, which is another pox-type virus that, while related to smallpox, can't cause it. It comes stored within a secure vial.

ANTIBODIES
With the vaccinia now in the body, it induces antibodies that are cross-protective for all variola (smallpox) viruses, as well as many others, including monkeypox and cowpox.

BLISTER
At the site of insertion, after four days a red, itchy bump develops, called the Jennerian vesicle. This blister fills with pus, then drains, dries and falls off eventually, leaving a scar.



PRICKING
The vaccinia solution is inserted by a series of quick, shallow pricks into the surface of the skin (usually on the arm). This causes a sore spot and draws a little blood.

NEEDLE
The smallpox vaccine is not delivered with a hypodermic syringe. Instead it is delivered using a bifurcated (two-pronged) instrument. The needle is designed this way so that it holds a droplet of solution each time.

1796
Edward Jenner realises that people infected with the non-fatal cowpox disease cannot catch any variant of smallpox. He proceeds to run a series of successful trials, creates the world's first vaccine and publishes his findings. He receives a very mixed reaction though.

1966
The Centers for Disease Control and Prevention (CDC) in Georgia, US, launches a campaign promoting the importance of smallpox and measles vaccinations. A series of posters is created and distributed globally.

1975
The last known person to have been infected with the naturally occurring variola major smallpox strain is treated. Rahima Banu Begum (right) fully recovers and is still alive today with four children.

1980
Thanks to Edward Jenner, numerous other scientists and organisations such as the CDC, smallpox is eradicated totally in 1980. Today, small stocks of the virus are kept in a few highly secure laboratories.

PIONEERING SCIENTISTS & MEDICS

MEET TEN MEDICAL MARVELS WHO HELPED TO TURN THE TIDE IN A TIME WHEN DISEASES LIKE POLIO, TB AND SMALLPOX STRUCK FEAR INTO COMMUNITIES

EDWARD JENNER
ENGLISH, 1749-1823

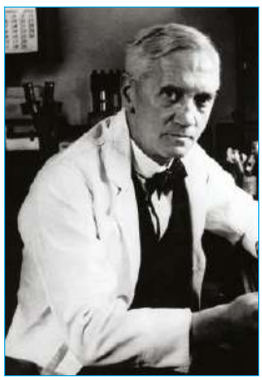
Smallpox killed millions across the centuries and was a particular danger to children but, thanks to Edward Jenner, the deadly disease was eventually eradicated. The doctor made his breakthrough in 1796 with an experiment on an eight-year-old boy, James Phipps. Taking pus from a cowpox pustule, he placed it in an incision in James' arm, proving there was truth to the old folk tale that milkmaids suffering from cowpox never contracted smallpox. Some were horrified by Jenner's methods – particularly the clergy, who pronounced it ungodly to inject humans with matter from diseased animals – but the vaccine became widely popular.

LOUIS PASTEUR
FRENCH, 1822-95

French national hero Louis Pasteur dipped his toes in many a scientific project and was a microbiology pioneer. The chemist's vaccines have protected millions, and his research into germ theory proved that food goes off due to contamination by microbes rather than miasma. Pasteur, who tragically lost two daughters to typhoid, made strides in tackling diseases such as cholera and rabies, while his former assistants Émile Roux and Alexandre Yersin assisted in the journey towards preventative action for diphtheria. Pasteur experimented on chickens when conducting his cholera tests, injecting them with old bacteria, which left them immune from fresh cholera intakes.

JONAS SALK
AMERICAN, 1914-95

Polio was widespread in the 20th century and it was the focus of much panic in post-war America. President Franklin Delano Roosevelt, who died in the final year of World War II, was thought to have contracted the disease himself, aged 39, and became paraplegic, though some today believe he was instead suffering from Guillain-Barre syndrome. Jonas Salk created the first successful polio vaccine in 1953, which was rolled out in 1955. The doctor, his wife and children had been among those to first test the formula. Cases of polio soon began to drop dramatically and its threat globally was significantly reduced.



ALEXANDER FLEMING
SCOTTISH, 1881-1955

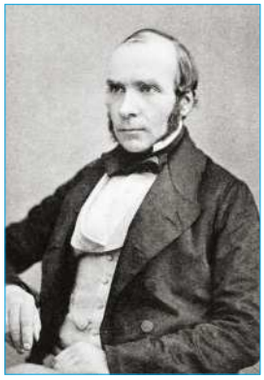
Known for his discovery of penicillin, Alexander Fleming was one of a flurry of innovators across the 19th and 20th centuries. The microbiologist, who researched causes of maladies such as tetanus and gangrene, stumbled across penicillin in 1928. Observing mould growing in a petri dish, he realised a culture of bacteria had killed the germs around it. The antibiotic was mass produced during World War II by Howard Walter Florey and Ernst Boris Chain, who came across Fleming's research when looking for such a treatment. Many lives were saved and the trio shared a Nobel Prize in 1945.

RHAZES
PERSIAN, 865-925 CE

Abū Bakr Muhammad Ibn Zakariyya al-Rāzī – known in the West as Rhazes – was the dominant scholar of early Islam. Inspired by Hippocrates and ancient Greek medicine, he wrote books on a variety of topics, including the *Al-Mansuri* and *Al-Hawi*, encyclopaedic reviews of medicine translated into many languages, which were then used as standard texts for Islamic and European students for centuries. Physician to the royal court and director of a Baghdad hospital, Rhazes presided over improvements including noting down patients' case histories and marking down symptoms of illnesses. His work on diseases saw him conclude that measles and smallpox were distinct afflictions.

ROBERT KOCH
GERMAN, 1843–1910

Described as the founder of modern bacteriology, it was Nobel Prize-winner Robert Koch who developed the first 'magic bullets' – chemicals formulated to attack specific bacteria. He proved a link between the bacteria *Bacillus anthracis* and anthrax through testing mice and created techniques of staining bacteria to improve visibility under the microscope. Koch and his team were able to identify bacterial causes for tuberculosis and cholera, and his methods inspired successors in the field.



JOHN SNOW
ENGLISH, 1813–58

John Snow was a giant in the Victorian era, seen as one of the founders of modern epidemiology. An experiment in 1854 linked a public water pump in Soho to an outbreak of cholera, confirming the physician's theory that the disease could be spread through contaminated water or food. Snow was a champion of anaesthesia and hygienic practices in the field, and he also designed a mask to administer chloroform after hearing of the drug's effectiveness.

JOSEPH LISTER
ENGLISH, 1827–1912

Joseph Lister was the champion of new cleaning practices in medicine and revolutionised surgical procedures in the process. He experimented with exposing wounds to chemicals – using dressings soaked in carbolic acid (phenol) – and found the chances of infection reduced significantly. Lister also introduced handwashing in a medical environment, the sterilisation of instruments and began spraying carbolic acid in theatre while operations took place. His simple but effective principles were adopted by numerous surgeons.

RONALD ROSS
ENGLISH, 1857–1932

Indian Medical Service doctor Ronald Ross, born in the country to a British family, was the man to prove the long-suspected link between mosquitoes and malaria. In 1897, Ross, a future Nobel Prize winner, dissected a mosquito that had fed on a malaria victim and found in its stomach the parasite previously observed by Alphonse Laveran and Sir Patrick Manson when they examined blood samples taken from others afflicted by the same disease.

ELIZABETH KENNY
AUSTRALIAN, 1880–1952

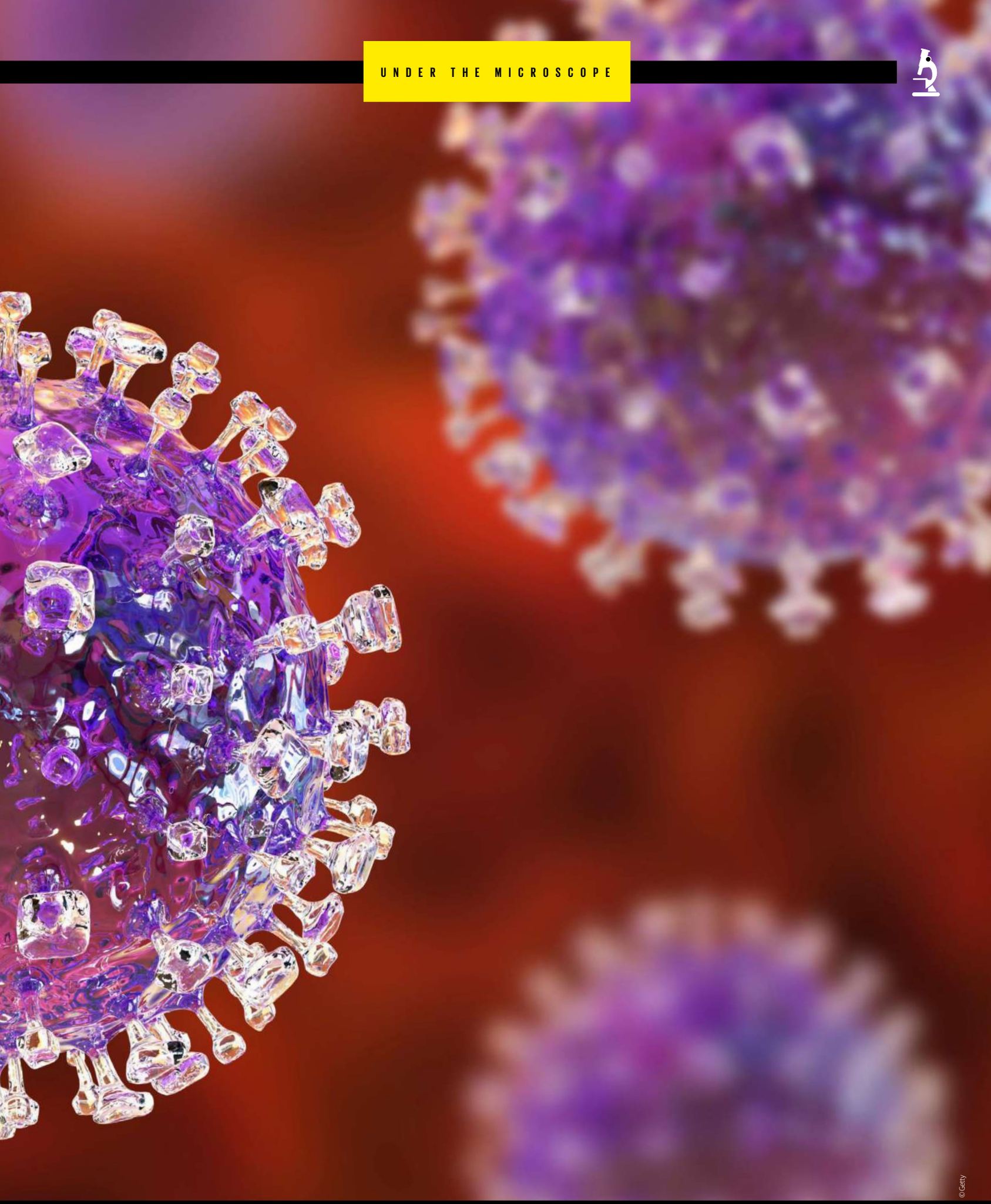
Elizabeth Kenny attracted acclaim and controversy in equal measure. Unsatisfied by traditional treatments for polio – centring on immobilisation through the use of plaster casts and splints – the Australian focused on efforts to 're-train' the muscles, using moist hot packs to reduce pain and allow limbs to be gently exercised. Although medical figures poured scorn on her methods, the public had a very different view. Kenny's practices are still used in rehabilitative medicine.

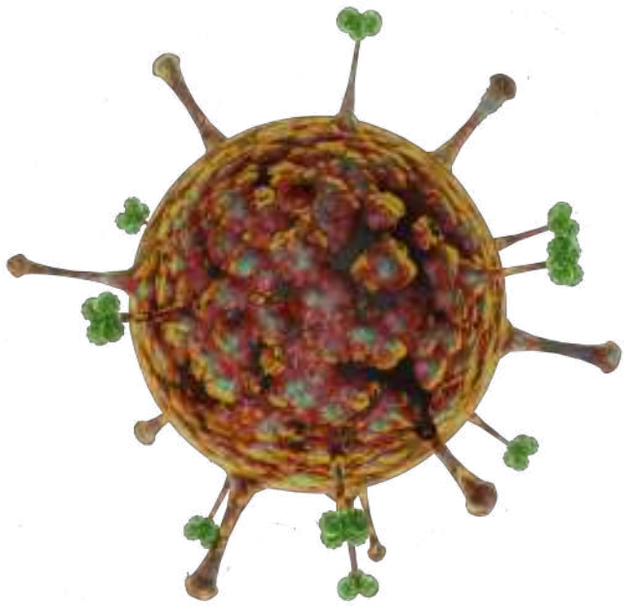
NIPAH

This lethal zoonotic virus (one that can be transferred from animals to humans) finds its natural home in fruit bats, but it can also be transmitted from pigs to people.

With a fatality rate of between 40 and 75 per cent, the symptoms of Nipah virus range from a fever, headaches and confusion to breathing difficulties, slipping into a coma and inflammation of the brain.

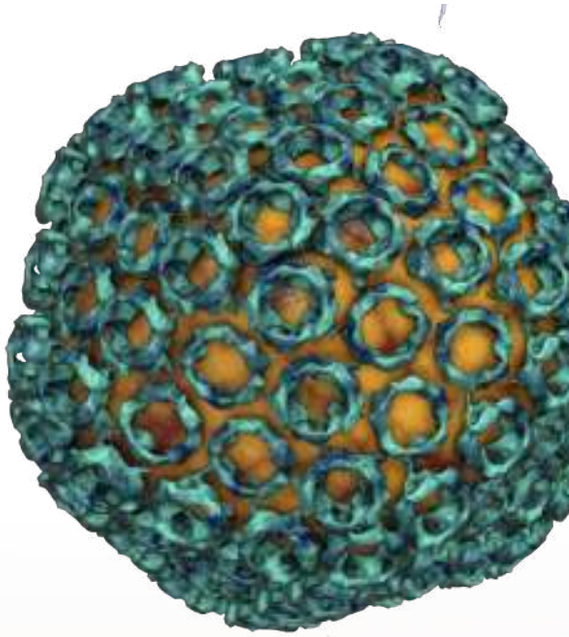
Outbreaks of Nipah have occurred in India, Bangladesh, Malaysia and Singapore, and while fatalities were generally low, the lack of a vaccine or any effective form of treatment has seen the virus placed on the WHO's priority list for further research.



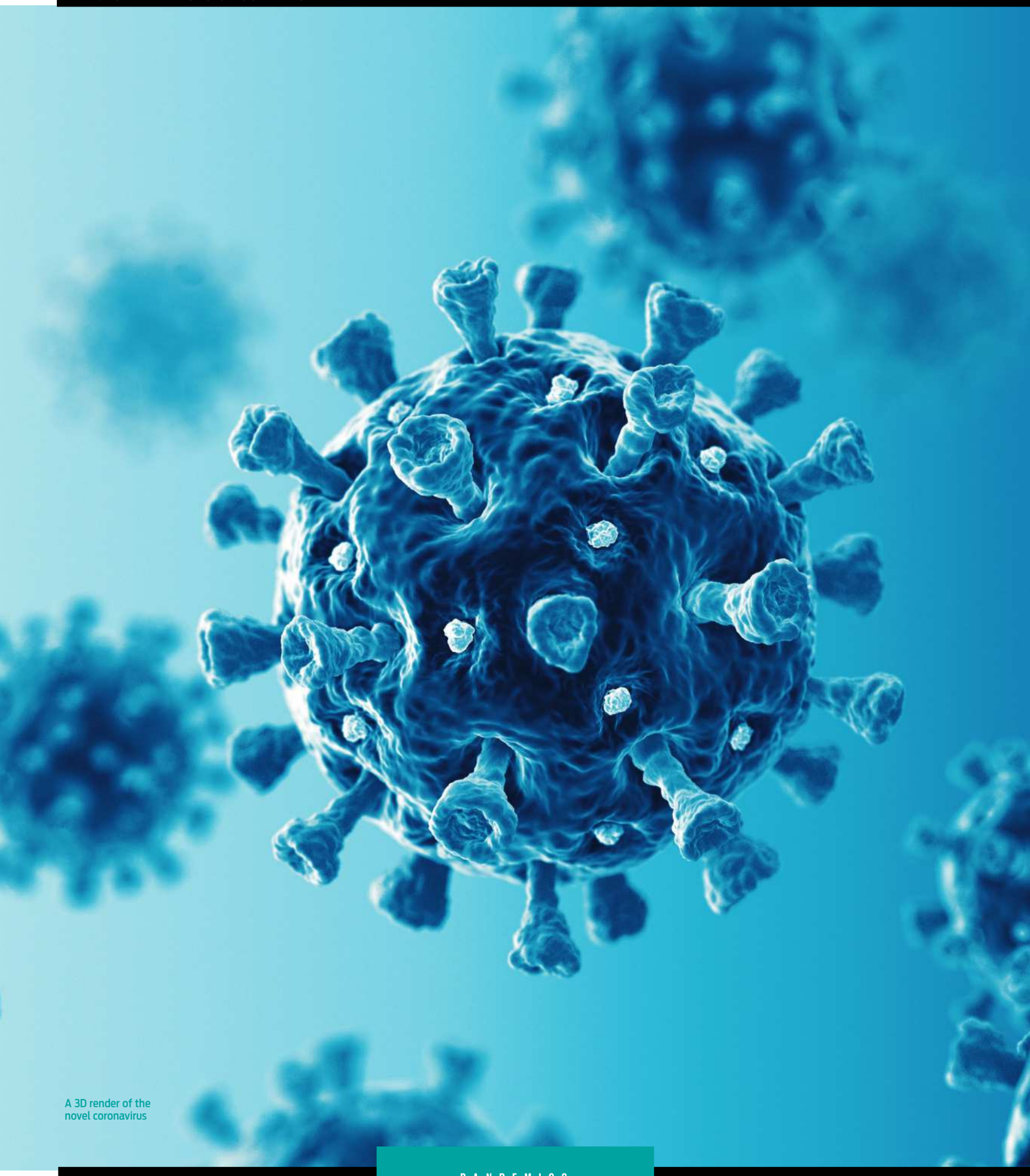


COVI

AND THE FUTURE OF VIRUSES



D-19



A 3D render of the novel coronavirus

PANDEMICS


© Getty

Disclaimer: The COVID-19 pandemic is ongoing and the situation can change rapidly. All are figures correct as of December 2021

THE GLOBAL EFFECTS OF COVID-19

CORONAVIRUS HAS SWEPT THE GLOBE, CAUSING DESTRUCTION IN MANY FORMS

WRITTEN BY **NIKOLE ROBINSON & CHARLIE GINGER**

The outbreak and deadly spread of COVID-19 has changed the world, and its effects are still ongoing today. Cases continue to rise, devastating families and disrupting livelihoods, with millions of jobs and industries impacted (some of the heaviest hit are events and hospitality, the arts, construction, real estate and the travel industry), placing strain on both the national and the worldwide economy and causing a catastrophic loss of life.

It all began in December 2019, when Chinese medical professionals noted a cluster of unusual, pneumonia-like cases in Wuhan City, Hubei Province, China. With several patients showing similar symptoms, the cause of the disease was investigated. On 27 December, Dr Zhang Jixian, head of the respiratory department at Hubei Provincial Hospital, reported to officials that he believed a new type of coronavirus was behind the symptoms, the newest member of a group of respiratory diseases. The Wuhan Municipal Health Commission alerted all hospitals in the province to look out for similar cases. A briefing was released online, confirming 27 cases, advising citizens to avoid public places and suggesting that face masks be worn outside – measures were already being put in place to try to block transmission. The World Health Organization (WHO) was notified as the number of cases crept up, and the Chinese Center for Disease Control and Prevention (CDC) received its first samples from four patients in Hubei to study the new virus.

COVID-19 is caused by the SARS-CoV-2 virus, which is able to spread between people who have been in close proximity – when someone carrying the virus has been in close contact with someone else. The virus spreads in liquid droplets released when an infected individual sneezes, coughs, talks or exhales. If these virus-laced droplets come into contact with a healthy person's eyes, nose or mouth it's highly probable that the virus will infect them too, with the likelihood of transmission increasing the closer they have been to the infected person. Crowded and unventilated spaces also make transmission more likely, as well as being in the same room as a carrier for an extended period of time, as some of the droplets are small enough to remain in the air and be breathed in.

Although the exact origin of the virus remains a mystery, several of the earliest cases have been traced to patients linked to 'wet markets' – markets that sell fresh produce such as meat, fish and fruit but that often also host clandestine exotic wildlife. Huanan Seafood Wholesale Market is believed to be the source of the novel coronavirus. The market was closed on 1 January 2020 due to this apparent connection, but the damage had already been done. As the cases slowly spread across the province, coronavirus claimed its first known victim on 11 January: a 61-year-old Chinese man who was known to frequent the market.

The first case outside of China was reported on 13 January when a 61-year-old woman in Thailand who had no connection to the wet market was diagnosed. Japan announced its first case just three days later, a day before a second in Thailand. With human transmission confirmed and four deaths reported in China, on 20 January the CDC categorised the coronavirus as a Class B infectious disease. While early measures, such as screening travellers, were put in place to stop the spread outside of Wuhan, cases cropped up in other cities including Beijing, Shenzhen and Shanghai. There were also cases reported in Hong Kong and Taiwan.

By the time the US announced its first case on 21 January – a man in his 30s who'd developed symptoms after returning from Wuhan – China's CDC had confirmed a total of 440 cases, with nine deaths. Despite the rise, at this time the WHO decided against declaring the outbreak a Public Health Emergency of International

Concern. China locked down Wuhan, closing shops and offices, making residents stay at home and cancelling transport in and out of the city. By 24 January, quarantine measures were extended to 12 Chinese cities, as the country's cases had almost doubled in just a few days. By the end of January there were cases dotted all over Asia, Europe and America. Borders began to close and travel was tightened, with the US and other countries putting a hold on flights to and from China after pulling out nationals.

Even with more stringent measures in place, the virus spread across continents, forcing the WHO to declare it a Public Health Emergency. All of the uncertainty around the virus - as well as lockdown measures forcing many businesses worldwide to grind to a halt or work in a reduced capacity - caused the most devastating fall in the global stock market since the Wall Street Crash in 1929, signalling the beginning of the COVID-19 recession. To date the cost of the pandemic to the global economy is in the trillions, with one estimate in October 2020 projecting losses of $16 trillion for the US alone, equivalent to approximately 90 per cent of the country's annual gross domestic product (GDP).

The UK has also experienced devastating financial losses. In 2020 GDP plummeted by 9.8 per cent, the worst economic constrictions in over three centuries. In a bid to prevent mass job losses as a result of the sudden downturn the government introduced a job-retention (furlough) scheme. While it did indeed save many from unemployment, it also cost the exchequer £68.5 billion to execute.

Fortunately, the UK experienced somewhat of a recovery in the summer of 2021, and by July GDP had bounced back to within two per cent of the pre-pandemic figure, and the good news isn't limited to the UK.

While there isn't a single national economy that has escaped the pandemic unscathed, J P Morgan has predicted a full global economic recovery in 2022, welcome news to businesses and employees the world over. However, what can never be replaced are the millions of lives claimed by the virus to date.

As of early December 2021, 265 million people across the globe have contracted COVID-19, with an estimated 5.3 million people having lost their battle with the virus. The worst-hit countries so far have been the US (813,904), Brazil (616,298) and India (474,211).

Europe has also suffered from several damaging waves. The UK has seen 146,135 deaths, and Italy, France and Germany have all lost over 100,000 citizens. As a result, various countries on the continent have reintroduced stern measures in response to rising cases and deaths, including restricting business opening hours, encouraging people to work from home if possible and insisting on the wearing of face

NO-FLY ZONE

TRAVEL AND TOURISM HAVE BEEN ONE OF THE INDUSTRIES WORST AFFECTED

Due to strict bans on travel starting in early 2020, millions of holidaymakers worldwide were forced to change their plans as trains, ferries and flights were cancelled and borders were closed. Only travel deemed absolutely essential was allowed. Between January and May there were 56 per cent fewer international travellers due to the restrictions imposed. While restrictions eased slightly over the summer and travel between certain nations was reopened – with these decisions usually based on the number of cases a particular country had at the time – many people were still too afraid of the risks to keep their plans in place. Many nations still require visitors to quarantine themselves for up to 14 days upon arrival to stop the spread of the virus, while others, such as Spain, have barred unvaccinated travellers from entering the country. While these measures are sensible, they have resulted in catastrophic losses in the tourism industry. Over 100 million jobs were lost in the sector in 2020, and the World Tourism Organization estimated that global tourism spending dropped between a staggering $910 billion and $1.2 trillion (approximately £680 billion and £896 billion). With international travel still limited going into 2022, these losses will only grow, and more and more companies will be put at risk.

© Getty

Planes have been grounded and borders have been closed

Good hand hygiene is the first line of defence against the spread of COVID-19

The first cases can be traced back to the Chinese city of Wuhan

This map highlights the distribution of cases around the world. The dots represent the total number of recorded cases in that region since the pandemic began.

A LARGER RED DOT INDICATES A HIGHER NUMBER OF TOTAL CASES IN THAT REGION, FOR EXAMPLE:

- 3,000,000
- 300,000
- 30,000

CASES BY COUNTRY

(WITH 1M+ CASES)

49,601,279	US
34,666,241	INDIA
22,167,781	BRAZIL
10,721,774	UNITED KINGDOM
9,752,340	RUSSIA
8,966,681	TURKEY
8,209,911	FRANCE
6,147,872	IRAN
6,386,758	GERMANY
5,348,123	ARGENTINA
5,273,178	SPAIN
5,164,780	ITALY
5,086,381	COLOMBIA
4,258,560	INDONESIA
3,908,534	MEXICO
3,760,048	POLAND
3,705,823	UKRAINE
3,093,452	SOUTH AFRICA

*Data provided by Johns Hopkins University. Accurate as of 21.10pm (GMT), 09/12/2021

masks. Yet while these methods have indeed played a key role in bringing case numbers back under control, the only solution that will enable societies across the world to get a permanent grip on the virus (most experts now agree that the complete eradication of the virus is virtually impossible) are successful vaccines.

As soon as it became apparent that COVID-19 was going to develop into a pandemic the race was on to find a way to immunise our bodies against it. Scientists in various locations worked tirelessly to isolate the spike proteins from the virus (which helps it to enter our cells but don't allow it to multiply or cause symptoms) so that these can be introduced to our bodies. By injecting people with a harmless coronavirus antigen, the defensive cells that protect our body against infection can learn to target and fight it without the risk of symptoms. This means that when the real virus enters the body, our cells kick into action and ward it off.

In what ranks as one of the finest chapters in the history of science, a number of highly effective vaccines were developed in a matter of months, the most prominent ones being the Moderna, Oxford/AstraZeneca and Pfizer/BioNTech vaccines (all three of which have been approved for administration in the UK). Yet the presence of a vaccine does not always necessarily equate to an immediate surge in immunity, as uptakes are varying wildly from country to country and even between cities and towns.

As of December 2021, over 55 per cent of the global population has received at least a single dose of a COVID-19 vaccine (two are required for enhanced immunity, with boosters also recommended to top up our defences), with over 8 billion doses administered so far. However, while these figures are impressive, and 32.3 million doses are now being administered daily, less than seven per cent of people living in low-income nations have been given a jab, and their are legitimate concerns about a growing chasm between wealthy vaccinated states and poor unprotected countries in which the virus will continue to flourish and claim lives. The amount of people living on a low income who have been vaccinated currently stands at 21.93 million. That figure rises to a truly staggering 1.7 billion for people subsisting on an upper middle income and stands at over 833 million for those on a higher income.

Another cause for concern in some areas is the notion of making vaccines mandatory, a controversial move that Austria has already adopted. Germany looks set to follow suit in early 2022, with its parliament poised to pass mandatory jabs into law.

According to Ursula von der Leyen, the President of the European Commission, the rest of the EU may yet have to adopt the same draconian measures in order to finally ward off the virus. Given the amount of protests and occasional outbursts of violence already directed at other social restrictions, it is likely that trying to enforce such methods will only lead to further unrest. And this isn't the only issue that governments in Europe and across the globe are now having to confront, for COVID-19 is still mutating, giving rise to new and potentially devastating variants.

In late 2020 the Delta variant was detected in India, and by 22 November 2021 it was present in 179 countries. It currently reigns as the world's dominant variant, but its position is now under threat from a potential usurper: Omicron.

The usually bustling streets of London were left deserted in lockdown

THE ANTI-VACCINATION MOVEMENT'S DANGEROUS IDEAS

HOW DENYING SCIENCE SPREADS DISEASE

The most heavily mutated version of the virus discovered to date, Omicron first emerged in South Africa and Botswana in November 2021, and it is rapidly catching up with its Delta cousin as it races around the world.

Now present in over 70 countries, it appears to be on the path to causing a fresh global wave, and while early evidence suggests that in order to become more transmissible (some sources have reported that Omicron is up to four times more transmissible than Delta in its early stages) the variant has had to sacrifice its lethality, this is yet to be confirmed, and the scientific community still has many questions to answer before the full extent (and threat) of Omicron is understood. It certainly seems to be very adept at bypassing its host's natural immunity (one study conducted in Israel found that six out of 11 people infected with Omicron had previously received three doses of the Pfizer vaccine, highlighting the variant's ability to swerve natural barriers).

Even so, the variant will still encounter the serious threat of people's T-cells set on destroying it, and those who have received a vaccine are less likely to suffer severely from COVID-19 in comparison to those who have not yet been vaccinated.

It remains to be seen how grave a threat Omicron is (most cases so far have thankfully been mild) and whether it will be followed by yet more variants, but what now seems certain is that the world will need to learn to live with this virus. The multi-pronged approach of vaccinations, social distancing, wearing a face mask in public and avoiding unnecessary travel will continue to be implemented across the globe for the foreseeable future. It is to be hoped that lockdowns can be avoided, for both the financial and mental welfare of citizens around the world, and that in time life can return to as close to normal as possible, with families, friends and colleagues reunited and the worst of COVID-19 a distant memory.

Despite the presence of numerous successful COVID-19 vaccines, there are many people who have decided they won't have it administered, in large part due to misinformation spread through social media. The Centre for Countering Digital Hate (CCDH) found in a survey that one in six Britons were unlikely to agree to be vaccinated, with around the same number yet to decide (to date over 39 million people in the UK are fully vaccinated). With so many unwilling to immunise themselves against the virus, herd immunity – which protects those who are medically unable to be vaccinated by making a certain amount of the population immune – may not be possible, and the virus will continue to spread.

The anti-vaccine movement had been problematic long before the spread of COVID-19 but has become troublingly widespread in recent years. Many of its supporters disregard the advice of medical experts and scientists in favour of unreliable sources, a lack of fact-checking and some truly wild theories, such as that the COVID-19 vaccine will microchip the population for tracking, or that it will alter our DNA. The anti-vax movement has already caused a resurgence of many diseases that had almost been eradicated through vaccination, such as measles and polio. The spread of misinformation – and, as a result, disease – through followers of this movement is truly deadly.

© Getty

INSIDE A CORONAVIRUS TEST LAB

MEET TWO SCIENTISTS FROM THE UK'S COVID-19 MEGALAB, HOME TO TEAMS WORKING AROUND THE CLOCK TO TEST THE PUBLIC


© Beth Cole


© Ben Galley

At the beginning of lockdown, virologist Ben Galley and neuroscientist Beth Cole were forced to stop all their practical work for their PhDs – but that wouldn't keep them out of the lab. Because of their laboratory experience they were asked to work on COVID-19 test samples, analysing swabs sent in by the public. During April and May, Ben and Beth swapped their smaller Leeds-based labs for a new COVID-testing 'megalab' in Milton Keynes.

WHAT WAS THE EXPERIENCE LIKE FOR YOU?

BETH: It was probably one of the most intense experiences of my life. It was good to be there and I was really happy that I was helping, but by the end I had to leave. The atmosphere and other people working there made it a good experience.

BEN: I really liked the sense of community. We were all there because we wanted to help. Although it was hard, it was nice that everyone was there wanting to do something good.

WHAT DID THE TRAINING INVOLVE?

BETH: We were meant to have a few days of training on each step, but because we started during a final push towards reaching 100,000 tests a day, they were really trying to get it off the ground. We were chucked in the deep end and trained on the job. In the first few days we tried all the stages. After the training, people knew what they liked, and the person in charge quickly identified which roles we were best at. I was quite fast at the first step and ended up staying there for ages.

BEN: First we had an induction day to get used to the environment and the setting. Then we would be trained in each stage of the process, with someone shadowing you and showing you how to do it. A lot of the jobs are repetitive, so there's not so much of a learning curve. Over the course of a 12-hour shift you end up being pretty good.

A DAY IN THE LIFE OF A COVID LAB SCIENTIST

AN AVERAGE DAY SHIFT AT THE UK BIOCENTRE

07:30-08:00
TEAM BREAKFAST
The 50 people working on the day's shift arrive from their hotel at around 07:30, where they are given breakfast to fuel the work ahead.

08:00-08:10
MORNING MEETING
The team finds out how many test deliveries they have been sent and are given an analysis of the previous day's shift. They can also talk through any problems that arose.

08:10
ASSUME POSITIONS
A whiteboard details the positions of everyone on the shift. As soon as they see their name and job, the lab workers make their way to their area and handover from the person finishing their shift.

12:00-13:00
LUNCH BREAK
This is the lunch slot for some of the workers, but to maintain a continuous process of testing not everyone can stop working at the same time.

18:00
EVENING MEAL
The length of this break varies, but it usually involves eating and returning straight to the job. The boss of the lab also reveals how many samples have been processed so far.

20:00
END OF SHIFT
The night-shift group take over. After leaving the lab, the team need to isolate themselves in the hotel until they return to the lab again.

HOW MUCH PRESSURE WAS THERE TO MEET A TARGET?

BETH: I found that the pressure was more external, coming from the news and the government. The people at the testing centre had more of an attitude of 'if you do it you do it'. They just wanted us to get as many tests done as we could.

BEN: Our boss was very results driven. That's important for the situation we were in, but it was very much that you had the minimum break, and often it was less than the minimum break. You would have to dash out, have a drink and come straight back. A 12-hour shift with no real break was very hard.

HOW MANY TESTS DID YOU PROCESS IN A DAY?

BETH: When I was on the first step, inactivating the virus, I had 94 samples on each plate, and it took between an hour and an hour and a half to do one plate. The most I ever did was around ten plates in a day. On my shifts we did around 20,000 tests. Milton Keynes was the biggest testing centre in the country, so our lab was a big chunk of the daily totals. The scientific process itself was quite fast, so I think the main delay in receiving results came from delivering the tests to the centre and then sending the results back.

WHAT DID YOUR ROLE INVOLVE?

BETH: We switched around stages, but I spent a lot of time on the first step, inactivating the virus. I opened the sample tubes and put the contents on a testing plate. This step could either be done by hand or by robots. I didn't really use the robots, but by the time I left they had doubled the number of robots to make things faster. While the robot was doing the work, you would always have to keep up with it, make sure all the lids were off and set up the tubes in place. You worked at the robot's speed, so it was manic.

BEN: We spent a lot of time on one particular process, but we were able to do all of them as they needed to make sure if people left, or became ill, they could slot another person into that role and it wouldn't slow down.

HOW ACCURATE DO YOU THINK THE TESTS ARE?

BETH: As time goes on they will definitely be getting more accurate, but when I was there they were still finding their feet with how the tests worked and what the good controls were to include. I don't know the percentage error at the moment, but when I was there I think it was a 30 per cent error rate. That's fairly high, but you have to remember that in normal science you do everything at least three times, whereas there you have one go at it. I do PCR tests a lot, and the threshold would usually be pretty high. But in this circumstance it was low because they wanted to account for any detection of the virus. There are a lot of factors that can influence a test, and I think when you do a test you should take it with a pinch of salt. You should question a negative result if you know you have symptoms.

HOW DIFFERENT WAS THIS LAB TO THE ONE YOU USUALLY WORK IN?

BETH: The main difference was that the implication of everything I did was a lot bigger. When I'm in the lab in Leeds, if I mess up it just gives me more hours of work, but in the COVID labs, that's a person's sample. Especially when it was whole care homes, you wanted it to be right. There's only one sample for each person, so you have to get it right the first time or that person has to do the test again, and I think it's quite a traumatic test.

BEN: You were very much a cog in the wheel. You were part of a process that worked, so you didn't have to improve it. Normally in a research setting I'm often tweaking it. If I do a practical and something isn't right, I can change it. That's a big thing in science, and I know a lot of people struggled with not being able to do that.

WAS THERE ANYTHING THAT SURPRISED YOU ABOUT THE MEGALAB?

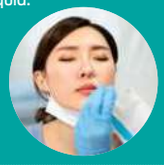
BETH: There was no PPE a lot of the time when we were all together. We had to wear PPE when we were handling the virus samples, but because we had to work really close together there was less focus on socially distancing with each other. I was surprised with how little thinking I was required to do. I remember thinking 'what if I don't know enough?' and 'what if I'm completely out of my depth?' but we just had to use manpower. I had also never seen such a big-scale operation, because I had always worked in really tiny labs.

BEN: The application said that you would need a lot of experience, but I met one person who started who was a college student, and she didn't even know how to pipette. That's no insult to her, because I didn't know how to pipette when I was a college student, but you don't expect a college student to be in a diagnostic laboratory working on the coronavirus. It was quite startling. I think that was a rarity though, and I like to think that when they started hiring people full-time they had a more thorough interview process.

TESTING FOR COVID-19

1. RECEIVING SAMPLES

Samples taken from patients' noses and throats are placed in a tube with half a teaspoon of liquid.



2. INACTIVATE THE VIRUS

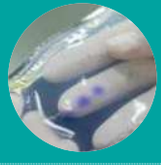
Sample tubes are opened and put into a plate with a lysis buffer. This is a chemical which breaks down any virus in the sample, making it safe while still detectable.

3. RNA EXTRACTION

After 20 minutes the virus is deactivated. It is then put in a machine that isolates the genetic information. This RNA is amplified to ensure any belonging to the coronavirus is detected.

4. POLYMERASE CHAIN REACTION (PCR)

Probes designed to bind to the virus' RNA alert the machine to the presence of the virus' genes.



5. READING RESULTS

The machine displays the amount of virus detected in a sample. Scientists record whether the number is above the threshold that determines a positive result. This limits the chance of a false-positive result.

Many effective Covid vaccines have been developed around the world

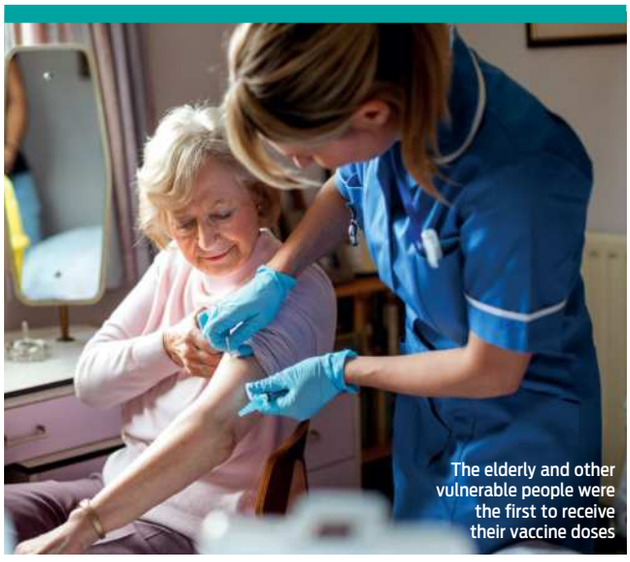
HOW THE CORONAVIRUS VACCINE WORKS

SEE HOW A TINY STRIP OF GENETIC CODE CAN HELP PROTECT US AGAINST COVID

The immune system is more than capable of suppressing the coronavirus, but first it needs some training. When the virus enters the body, the first thing the immune system needs to do is work out what it is. To do this it sends in foot soldiers, called macrophages, which eat up the remains of infected cells and break them down into pieces called antigens.

The macrophages take these antigens to the nearest lymph node for analysis. There, thousands of immune cells called T cells and B cells pile in to have a look. T cells come in two types: killers, which specialise in killing virus-infected cells, and helpers, which release chemicals to boost the immune response. The B cells are primed to make antibodies, which target virus particles like homing missiles. But there's a catch: there are millions of T and B cells in the body, and each one is slightly different. Only a handful are able to tackle a coronavirus infection. To fight the virus effectively, the immune system needs to find that handful of specialised cells and clone them to make an army. This process takes around seven days, by which time some people are already very sick.

Vaccinations give the body a chance to get this training process out of the way before it encounters the real virus. The new coronavirus vaccines do this by giving the body virus antigen - or the instructions to make it - without any of the rest of the virus. This means that the immune system can find the right T and B cells, and get them ready, without having to worry that the virus is multiplying. The antigen the vaccines focus on is called the 'spike protein', which is the protein the coronavirus uses to get inside human cells. Once the immune system has learnt to target this protein, it can stop the virus in its tracks.



The elderly and other vulnerable people were the first to receive their vaccine doses

TOP FIVE VACCINES OF ALL TIME

1. SMALLPOX
This deadly disease was completely eradicated by a vaccination program in 1979. It is the first and only human disease ever eliminated in this way.

2. RINDERPEST
This cattle plague virus used to wipe out entire herds of cattle and buffalo, causing devastating famines. In 2011 it became the first animal disease ever eradicated by vaccination.

3. POLIO
Polio is set to be the second human disease eradicated by vaccination. It has almost completely disappeared in most parts of the world, and efforts to totally wipe it out are underway.

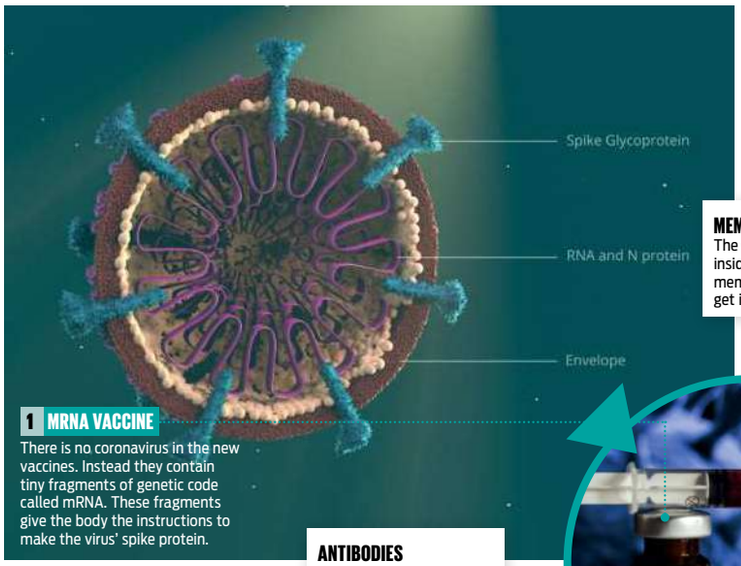
4. MMR
The triple vaccine against measles, mumps and rubella has saved thousands upon thousands of lives. The measles vaccination alone has saved over 20 million lives between 2000 and 2015.

5. FLU
The flu vaccine is an annual feat of human ingenuity. With circulating viruses constantly changing, scientists predict the strain we'll need protection from a whole year in advance.

5. READING RESULTS
The machine displays the amount of virus detected in a sample. Scientists record whether the number is above the threshold that determines a positive result. This limits the chance of a false-positive result.

WHAT IS AN mRNA VACCINE?

PRIMING THE BODY WITH VIRAL GENETICS TEACHES THE IMMUNE SYSTEM HOW TO FIGHT BACK



1 MRNA VACCINE

There is no coronavirus in the new vaccines. Instead they contain tiny fragments of genetic code called mRNA. These fragments give the body the instructions to make the virus' spike protein.

MEMBRANE

The vaccine is packaged inside bubbles of membrane to help it get inside human cells.

2 INJECTION

Like many other vaccinations, the coronavirus vaccine enters the body via an injection into the muscle in the upper arm.

3 ANTIGEN MANUFACTURE

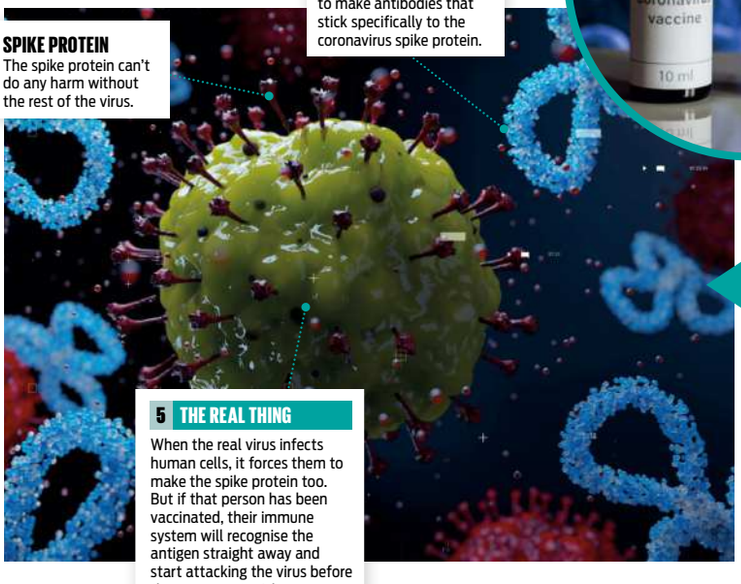
The vaccine enters cells in the arm, delivering the mRNA. The cells then read the coded instructions and start making coronavirus spike proteins. They put the finished proteins on their surface for the immune system to see.

ANTIBODIES

The immune system learns to make antibodies that stick specifically to the coronavirus spike protein.

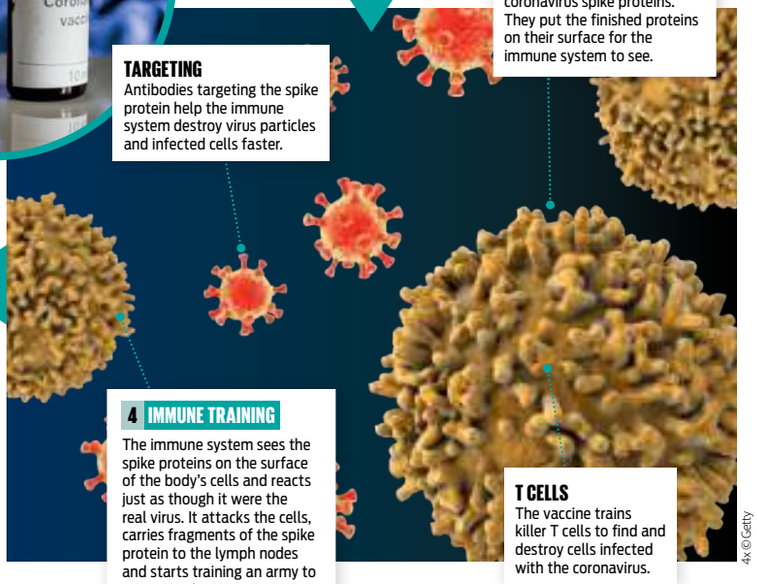
SPIKE PROTEIN

The spike protein can't do any harm without the rest of the virus.



TARGETING

Antibodies targeting the spike protein help the immune system destroy virus particles and infected cells faster.



5 THE REAL THING

When the real virus infects human cells, it forces them to make the spike protein too. But if that person has been vaccinated, their immune system will recognise the antigen straight away and start attacking the virus before the person gets sick.

4 IMMUNE TRAINING

The immune system sees the spike proteins on the surface of the body's cells and reacts just as though it were the real virus. It attacks the cells, carries fragments of the spike protein to the lymph nodes and starts training an army to recognise the virus.

T CELLS

The vaccine trains killer T cells to find and destroy cells infected with the coronavirus.

4x ©Getty

WHAT IS HERD IMMUNITY?

A virus can only transmit from one person to the next if the immune system of the uninfected person doesn't know how to fight it. As soon as the immune system learns to attack the virus, the chain of transmission stops. The more people who have a vaccination, the harder the virus finds it to infect a new host. 'Herd immunity' is the point at which so many people are immune to the virus that it can't find anyone new to infect. Once this point is reached, transmission of the virus all but stops.

The great thing about herd immunity is that not everyone needs to be immune to the virus for the whole population to be protected. If most people have a vaccination, it makes it harder for the virus to find the remaining unvaccinated people. This means that people who aren't able to have a vaccination for medical reasons can still be protected.

If enough people develop immunity, the virus will stop spreading

©Getty

Scientists hope the vaccines can be adapted relatively quickly to protect against any new variants that emerge

©Getty

INFLUENZA

This annual visitor infects around eight per cent of the US population every year, such is its virulence. A constantly adapting threat, scientists have to create a new vaccine every year in order to combat the flu's latest arsenal.

Known to cause side-effects including headaches, fever, a sore throat, fatigue, muscle pain and, in some severe cases, vomiting and diarrhoea, influenza kills thousands of people every winter, highlighting just how vital it is that those who are most vulnerable are vaccinated.

THE WHO'S WAR ON VIRUSES

WHICH DISEASES ARE CURRENTLY ON THE WATCH LIST AS THE WORLD'S NEXT GREATEST KILLERS?

WRITTEN BY **AILSA HARVEY**

As the COVID-19 pandemic has demonstrated, viral outbreaks can be fast-paced, unpredictable and unforgiving. For scientists specialising in infectious diseases, there is always more to learn, and this is done through monitoring the patterns in infection and keeping a close eye on the ever-changing pathogen population. The planet is packed with them, and there are more emerging all the time. At the current rate, a new disease is discovered every year, and it is the job of the World Health Organization (WHO) to accumulate all the data they can.

For the most successful viruses, their destructive multiplication won't go unnoticed. Because outbreaks can be rapid, the challenge for scientists is to place themselves one step ahead, working out which are the biggest killers with the greatest epidemic or pandemic potential. The viruses featured on the following pages are the ones the WHO have chosen to focus the majority of their time and resources on in the hope of being as prepared as possible when disaster strikes again. This list includes not only the established viruses but also one unnamed threat to the human population that may yet emerge.

A WHO worker decontaminates the house of a positive-testing pastor in the Democratic Republic of Congo during the Ebola outbreak of 2014–2016

© SOPA Images/ Getty Images

1

LOCATION
Nigeria

DATE OF DISCOVERY
1969

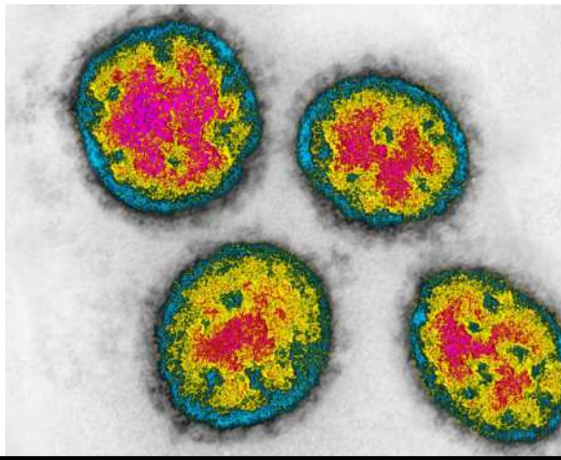
DEATH TOLL
5,000 deaths per year

VIRUS
LASSA FEVER

Lassa fever is endemic in areas of West Africa, having originally been passed to humans from multimammate rats. Usually, human cases are linked with coming into contact with the infected rats' urine or faeces, either ingested with their food or lingering on household items. Less commonly, transmission between humans can occur, but so far this has mainly been limited to within poorly sanitised healthcare facilities.

Upon infection with Lassa fever, sufferers usually become ill between six and 21 days later. Early signs include nausea, vomiting, headaches and swollen glands. As well as a hemorrhagic fever, the severe symptoms are bleeding from internal organs and swelling of the neck and face. The blood vessels in the patients' organs eventually become so damaged that the body struggles to support itself. However, 80 per cent of those with the virus will show no symptoms at all. If this virus is attended to promptly, the chance of death is low. Knowledge of the virus continues to increase, and the fatality rate has reduced to one per cent of Lassa fever sufferers.

The incubation period for the pathogen can range from two to 21 days. Scientists discovered that rats can keep hold of this virus for the rest of their lives, meaning that for as long as they are around, so is the threat of Lassa fever.



2

VIRUS

MERS & SARS

Coronaviruses are a large family of viruses that can cause respiratory and intestinal illnesses in animals and humans. Usually, these viruses only present themselves as mild and manageable colds, but two of the coronaviruses on the WHO's list, MERS and SARS, show how viciously these pathogens can attack the respiratory system.

MERS (Middle East respiratory syndrome) is transferred to humans from dromedary camels, while SARS (severe acute respiratory syndrome) came from civet cats. Because there is no vaccine available for the two, and because they can be easily spread between humans, the viruses remain monitored.

MERS was first detected in the sputum sample of a 60-year-old after his death and caused five people to die within the following month. Since then, it has spread to 27 countries around the world, but only 20 per cent of all cases have occurred outside Saudi Arabia.

Meanwhile, in March 2003, the WHO decided that it was global air travel that was creating a worrying spread of SARS. Just three days after issuing a global warning of an unknown disease among hospital staff, SARS was named and those with symptoms were advised not to travel. An epidemic was announced in July of that year and since then there have been four smaller outbreaks. Although they haven't taken hold of the world, these cases are enough for the WHO to make SARS a priority. The organisation is working to produce vaccines for animals to stop initial zoonotic transmission and human vaccines both for long-term control and for instant reactions in outbreak settings.

LOCATION

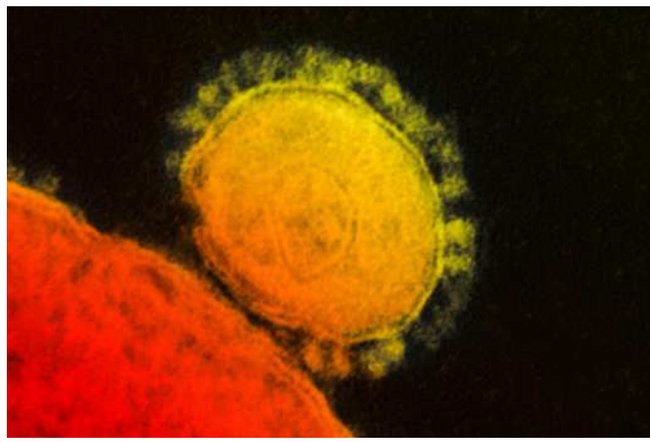
MERS Saudi Arabia
SARS China

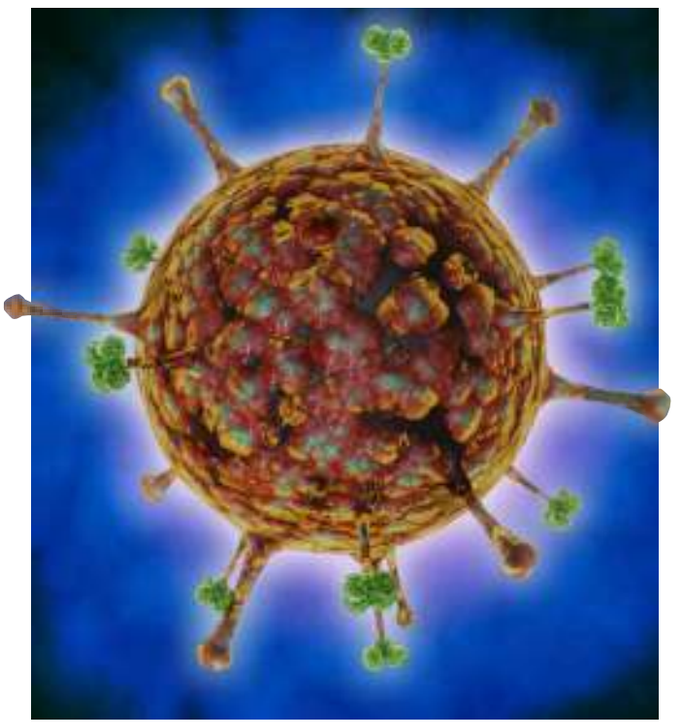
DATE OF DISCOVERY

MERS 2012
SARS 2003

DEATH TOLL

MERS 866
SARS 774





3

VIRUS

NIPAH & HENIPAVIRAL DISEASES

Nipah virus is one of only two henipaviruses that is passed to humans from animals. It can cause inflammation of the brain and comes mainly from pigs and fruit bats. However, one of the vital factors that sees this virus placed on the list is the vast range of animals that can carry the disease, maintaining an ongoing background existence, even when human cases are low. With no effective treatments for Nipah virus, the only measures that can be taken to reduce cases and the spread between people are to keep sick animals away from communities and to avoid anything that could be contaminated by animals with the disease. This includes staying away from food and water that bats have touched, especially raw palm sap. Through research so far the only medication that has had any sort of positive reaction in fighting Nipah virus is the antiviral ribavirin.

The outbreaks of Nipah virus in two regions of India – Kozhikode and Malappuram – killed 17 of the 18 who contracted it. This high death rate put the disease in the spotlight in May 2018. Most of these cases were passed on to healthcare workers and their families, and while the WHO sees this as lower risk in terms of human-to-human transmissions of the pathogen around the globe, the possibility of fruit bats spreading it during migration is concerning.

LOCATION

Malaysia

DATE OF DISCOVERY

1999

DEATH TOLL

<300

DISEASE X

One disease stands out from the rest on the WHO's list: Disease X. This represents an as yet unknown risk to the public. While many of these dangerous viruses can be monitored and their progression tracked, Disease X is an unforeseen pathogen that will arise in the future. It is a potential global emergency waiting to happen – we just don't know when or what it will be. Yet even without knowing its capabilities, medical professionals keep this pathogen on the list as a reminder to remain prepared.

Without any data, it is impossible to form specialised responses, so the WHO needs to prepare for a Disease X epidemic more generally. What makes many epidemics and pandemics so destructive is the element of surprise, coming out of nowhere when our defences are limited. General disease preparation can be more flexible, allowing plans to be tailored when more specific information is presented.

The WHO's first method of control is surveillance. Unusual changes in climate, healthcare trends and animal behaviour can become opportune environments for pathogens to grow. Next, the organisation needs to work on improving healthcare in some of the most neglected communities. This will help when it comes to stabilising any prevalent pathogens.

Finally, with vaccines being the most effective way to build our immunity to specific viruses, research and development laboratories and vaccination supply chains need to be established and then continuing to explore their versatility. This way, when Disease X is revealed, these systems will be in a better place to adapt and distribute solutions.

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4

VIRUS

CRIMEAN-CONGO HEMORRHAGIC FEVER

As a tick-borne disease, Crimean-Congo hemorrhagic fever (CCHF) is widespread within these animals throughout Africa, Asia, the Middle East and Europe. It can cause sufferers to experience fever, dizziness, muscle pain, sickness and confusion. With a 30 per cent death rate, those who lose their lives to this virus usually do so during the second week of illness. Otherwise, patients will begin to see improvements after around nine or ten days of displaying symptoms.

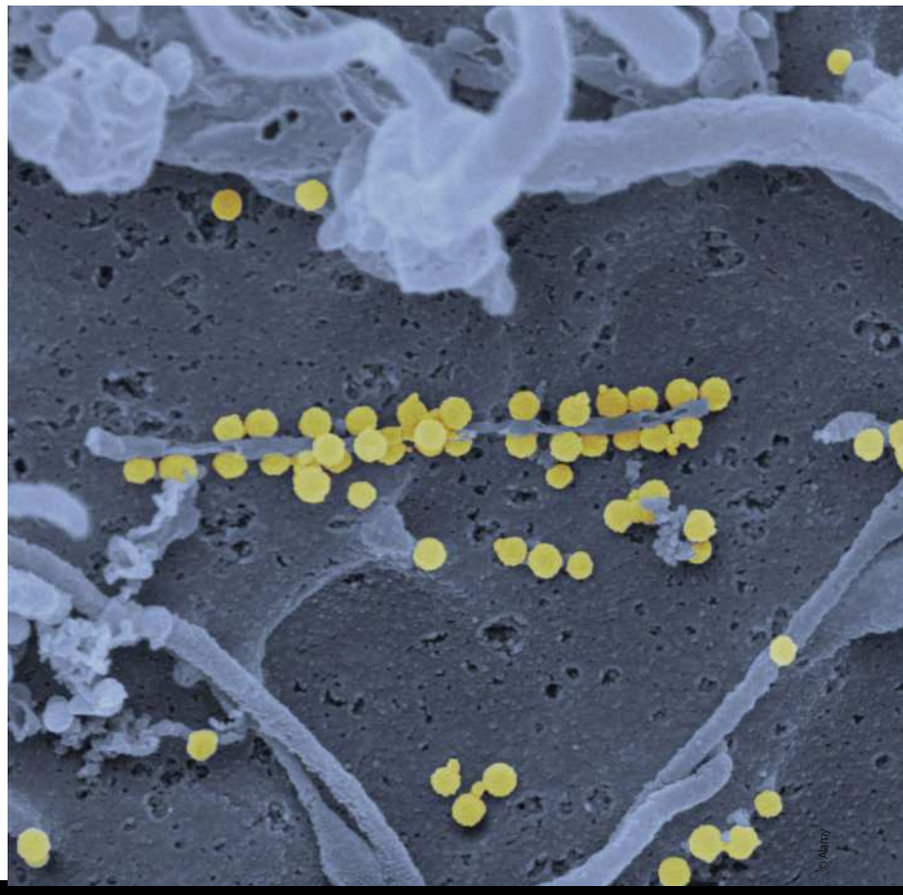
It's because of its prevalence across continents that this disease demands surveillance. It is the most widespread of all tick viruses that impact humans and is passed on either by being bitten by an infected tick or coming into contact with the bodily fluids of another infected animal. After transmission, CCHF can remain in the bloodstream for one week. During this time, the disease can be carried on by the next tick that bites the individual, increasing the percentage of infected animals in the area.

Although ticks seem to be the main transmitters, there is limited knowledge surrounding CCHF, despite the fact that it has successfully spread itself across large parts of the globe. The WHO are focusing on this virus in order to understand it better and improve diagnostic tests. Its true dangers can't be seen without more accurate and well-researched tests. Currently, one of the biggest drawbacks is the need for specialised technical equipment for handling the infectious specimens. This makes it difficult to roll out enough accessible tests to keep infections under control.

LOCATION
Crimea Ukraine

DATE OF DISCOVERY
1944

DEATH TOLL
Unknown
(10–40% death rate)



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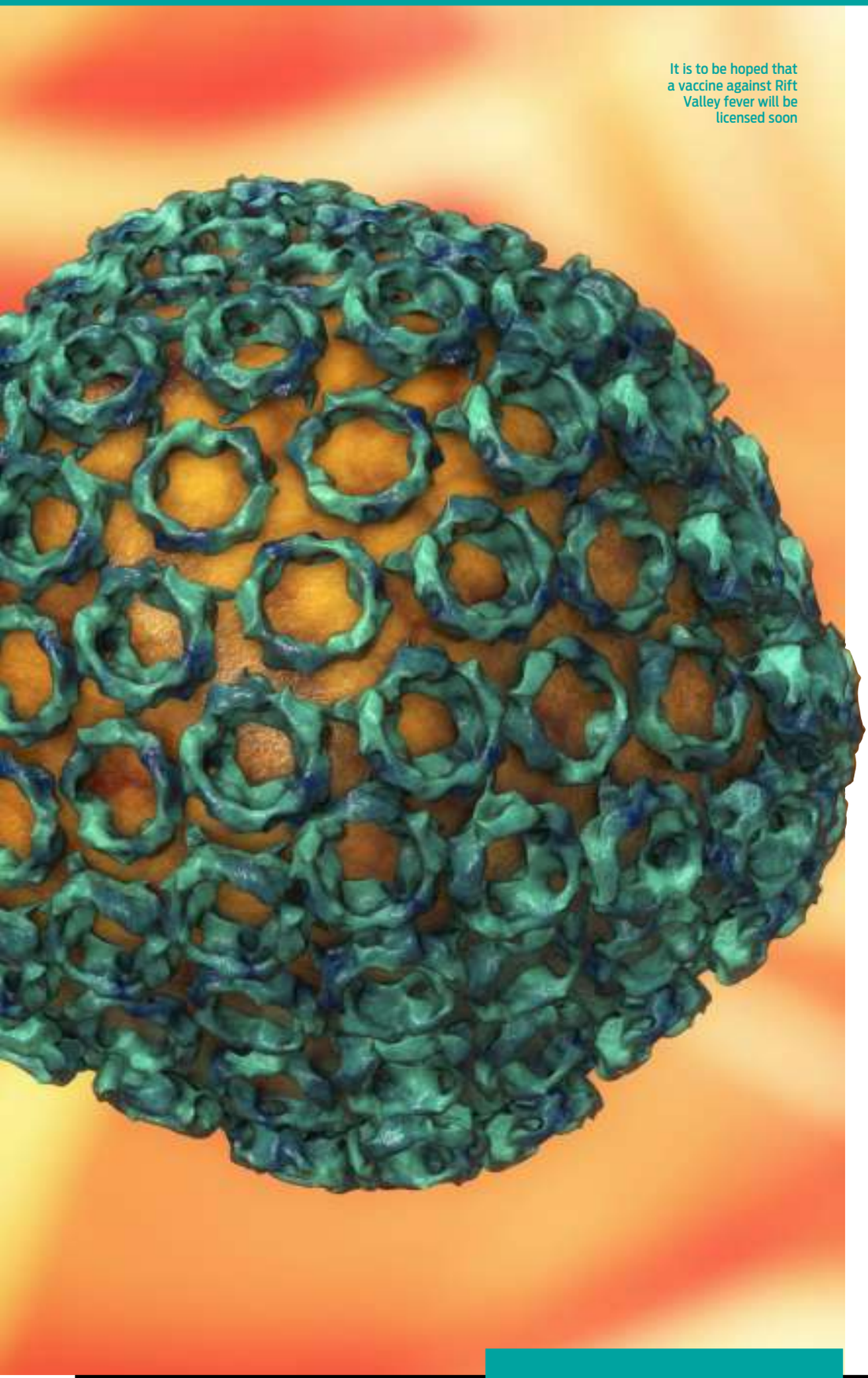


It is to be hoped that a vaccine against Rift Valley fever will be licensed soon

5

LOCATION
Kenya

DATE OF DISCOVERY
1931

DEATH TOLL
1,400+

VIRUS

RIFT VALLEY FEVER

Named after the area of Kenya it originated from, Rift Valley fever is a Phlebovirus that is hosted by blood-feeding flies such as mosquitoes. Mostly, the virus targets other animals, and the main issues are economic due to the loss of livestock. However, outbreaks within the human population have occurred from flies or through contact with the blood of infected livestock. For that reason, farmers and slaughterhouse workers are usually the most at risk. Serious forms of this disease can result in blindness, neurological complications such as memory loss, and internal bleeding.

In 1997, this disease escalated, with 90,000 people in East Africa testing positive for the virus in the space of only three months. During this time 500 people died. This was just one of multiple outbreaks, and so even though a vaccine has now been produced with positive results, the WHO's research is ongoing. Studying the patterns of outbreaks, the prime time for its spread has previously been following periods of heavy rainfall. This is due to the damp environments providing the ideal nesting ground for mosquitoes. Equipped with this knowledge, scientists are using NASA's data of changing ocean temperatures in order to predict weather patterns and, in turn, the likelihood of a Rift Valley outbreak.

There is a vaccine currently being used by humans to prevent Rift Valley fever, but this inactivated vaccine is not commercially available. Tests are continuing to improve its safety and effectiveness, but the vaccine has had apparent success when being given to those who work closely with the virus. Other potential vaccines are also being investigated with the hope that one will be licensed soon.

6

VIRUS

EBOLA AND MARBURG

These viruses are both considered to be rare diseases of the same group, but they have the ability to develop into devastating outbreaks. Scientists now believe that these diseases hold low contagion risk until symptoms begin to show, making them easier to track. Knowledge of how these are spread is most important in order for those in at-risk areas to take precautions. The viruses can't be passed on through the air but through infected blood and waste products.

Marburg and Ebola both have extremely high death rates, with up to 90 per cent of those infected losing their lives. In reported Marburg cases, most can be traced back to a visit to a mine or cave where Rousettus bat colonies reside in Uganda. It only takes one person to enter a disease-riddled cave and become infected to spread it to many. Fevers, headaches and muscle pains can occur quickly as a result, with complications leading to bleeding and organ failure. These symptoms can be difficult to tell apart from those of other viral hemorrhagic fevers, but antibody and antigen tests have been able to confirm whether the immune system has come into contact with these particular strains before.

26 outbreaks of Ebola have taken place in ten African countries since it was discovered. The latest long-term case lasted for two years. It came to an end during June 2020, but became increasingly severe and difficult to manage as it continued to infect people at the centre of a warzone. Sufferers of Ebola and Marburg are often treated to reduce any complications, but this doesn't cure the disease. Thanks to Ebola being prioritised, the first vaccine was approved last year. Use of the vaccine (made by Merck & Co, Inc.) resulted in the Democratic Republic of Congo declaring an end to its latest outbreak in November.

LOCATION

Ebola Democratic Republic of Congo

Marburg Germany and Serbia

DATE OF DISCOVERY

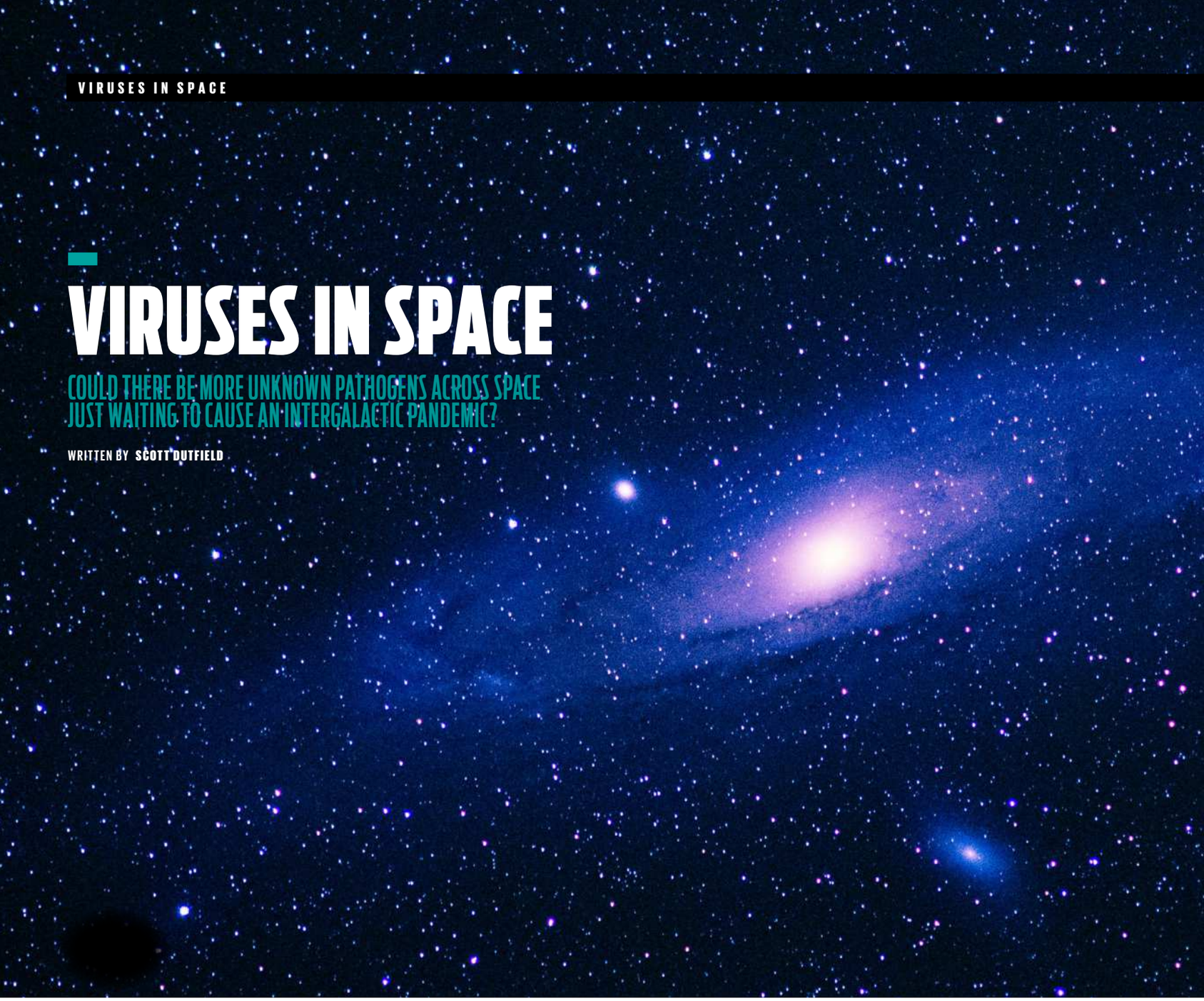
Ebola 1976

Marburg 1967

DEATH TOLL

Ebola 2,299

Marburg 470+



VIRUSES IN SPACE

COULD THERE BE MORE UNKNOWN PATHOGENS ACROSS SPACE JUST WAITING TO CAUSE AN INTERGALACTIC PANDEMIC?

WRITTEN BY **SCOTT DUTFIELD**

Viruses are the most abundant form of 'life' on Earth and have been populating the planet for around 3.4 billion years. But have they spread out into space?

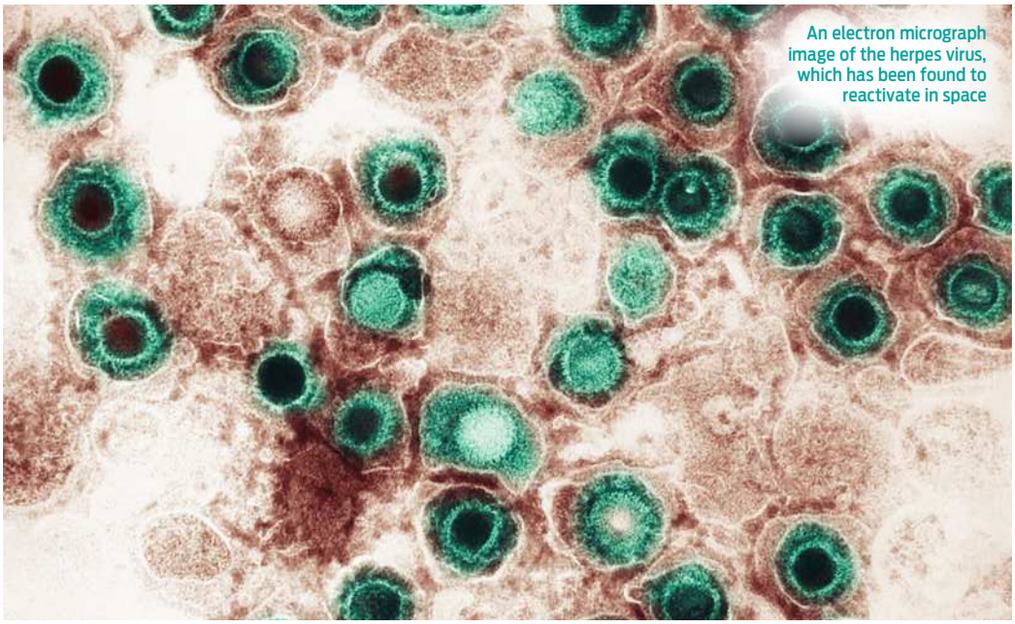
Scientists have discovered more than 4,000 exoplanets (planets outside our solar system) that are capable of housing extra-terrestrial life, with some reports suggesting a potential 60 billion more across the galaxy. Theoretically, if a planet has hosted life resembling any stage of the evolutionary journey on Earth, there's a fair chance that viruses call it home too.

Researchers in the field of astrobiology – a branch of science that studies the origins, evolution and future of life across the universe – have begun turning their attention to 'astrovirology' in recent years, as humankind's frontier into space expands. However, thus far evidence of any extraterrestrial viruses is non-existent. One of the major reasons for this lies in the technicality of virus hunting in space. A virus is microscopic, ranging from 20 nanometres to over one micrometre in diameter. To detect them, a transmission electron microscope would be needed, but these are in short supply for space exploration.

Cellular life releases detectable chemical by-products through biological processes such as respiration and digestion, and these gases can be detected from Earth and can help pinpoint where life in the universe might be. Viruses, however, release no such detectable by-products. Although there might be scope to find viruses on a far-off planet, the chances of them drifting through the dark abyss of space or even falling to Earth are slim to none.

Scientists know that viruses are no more than a bundle of proteins and genetic information that replicate within a host's body. Outside of that body, a virus only has a small window of opportunity to find another host before it dies. On Earth, for some viruses such as the flu, this window will last several hours, but for others, such as COVID-19, it can be several days. However, a virus floating in space has no such window to stumble across a living host to infect. Also, in outer space the temperature plummets below -270˚C and although viruses typically thrive in colder conditions, the frigid expanse of deep space would likely render them useless.

Although the research into alien viruses is generally woefully lacking, there are calls for



An electron micrograph image of the herpes virus, which has been found to reactivate in space

An artist's illustration of Kepler-1649c, an Earth-like planet that could be the best contender to host undiscovered life

© NASA/Ames Research Center/Daniel Rutter

change, possibly exacerbated by the stark reality of the COVID-19 pandemic. One of the main reasons astrobiologists are making space viruses a priority is due to humankind's far-reaching exploration of space. Although to date man has only set foot on the Moon, space travel giant Space X, founded by tech mogul Elon Musk, aims to put footprints on the dusty surface of Mars by 2030. How any viruses brought to Mars from Earth would react on the surface of the Red Planet remains a mystery. Similarly, any unknown Martian viruses making their way back to Earth, possibly hijacking a ride on a returning space rover, pose the same concern.

In early 2020 a report was published by Stanford University, US, that outlined their recommendations for "planetary protection" to prevent cross-contamination between Earth and other planets during humankind's continued exploration of the cosmos. From heat sterilisation treatments to extraterrestrial containment zones, the report details how space entrepreneurs such as NASA and Space X can prepare for potential alien virus exposure.

Although astrobiologists don't know much about potential alien viruses on other worlds, what they *have* discovered is that pathogenic hitchhikers from Earth act very differently during spaceflight.

Astronauts and space equipment undergo rigorous sterilisation and decontaminating processes before and after escaping the gravitational grip of Earth. However, some viruses such as herpes, chickenpox and shingles have made their way into space in the bodies of their astronaut hosts. On Earth, these kinds of 'dormant' viruses typically remain in the human body, producing no symptoms and being kept in check by our immune systems.

After testing the urine, blood and saliva samples of astronauts, researchers have found that mankind's immune system isn't as effective at keeping persistent pathogens at bay during spaceflight, with some astronauts even exhibiting symptoms of herpes. In a study of 89 astronauts, six experienced herpes breakouts in space. It's thought this may be due to the release of stress hormones, such as cortisol, which naturally lower the body's immune system. This type of research is invaluable in preparing for humankind's journey through the stars and how our bodies might react to new worlds.

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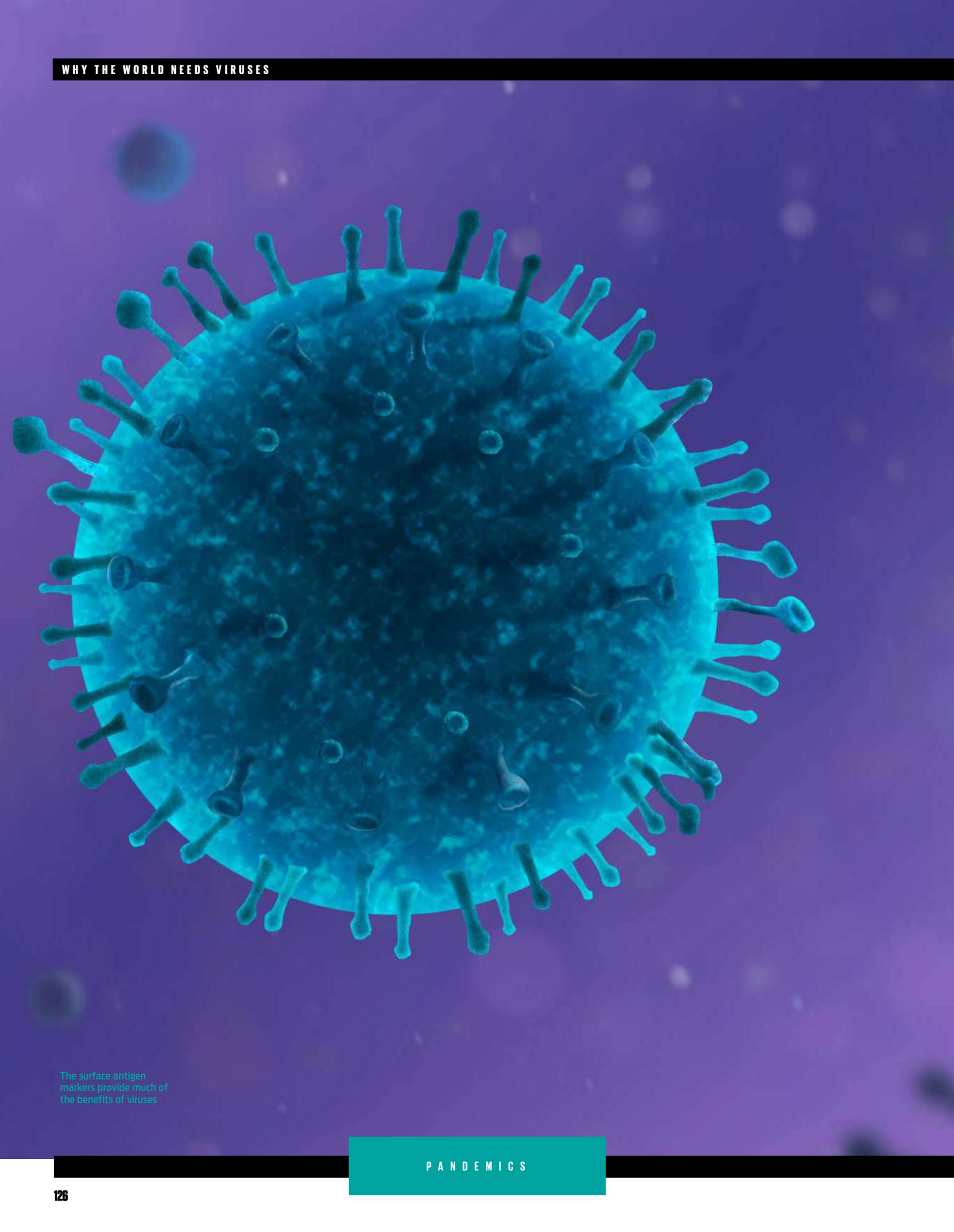
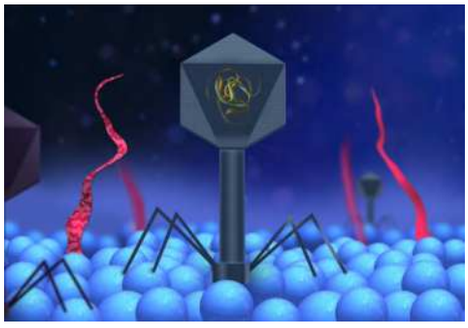


The surface antigen markers provide much of the benefits of viruses

WHY THE WORLD NEEDS VIRUSES

WHILE VIRUSES HAVE A BAD REPUTATION, EARTH WOULD BE A WORSE PLACE WITHOUT THEM

WRITTEN BY **PETER FENECH**



Viruses are mysterious entities and are more often than not considered to be sinister, invisible enemies that should be feared. In the current climate of the COVID-19 pandemic and the heightened awareness of the devastating consequences of uncontrolled viral spread, this is understandable. However, not every virus is pathogenic to humans – there are many species that either have a neutral relationship with us or, as we will explore here, can actually benefit us on several levels.

From the moment we are born we're exposed to viruses from multiple sources on a daily basis – from airborne particles to those on the surfaces we come into continuous contact with. It is this contact that enables our immune systems to become properly tuned to deal with the infectious agents we will encounter throughout our lives. This effect can be both generalistic in nature and, at times, highly specific. Having viruses in our bodies at a systemic level, but at low concentrations, keeps the immune response primed for invasion by more problematic organisms. In other cases, the nature of a non-symptomatic virus can lead to resistance to particular strains of infectious species that have similar antigens – the markers of a foreign organism, which stimulate an immune response. While the intent is entirely selfish – the aim is to remove competitive viruses and allow the host to support the non-pathogenic strain for longer – the effect is undoubtedly useful from our perspective. Without this process we would struggle to survive far beyond childhood.

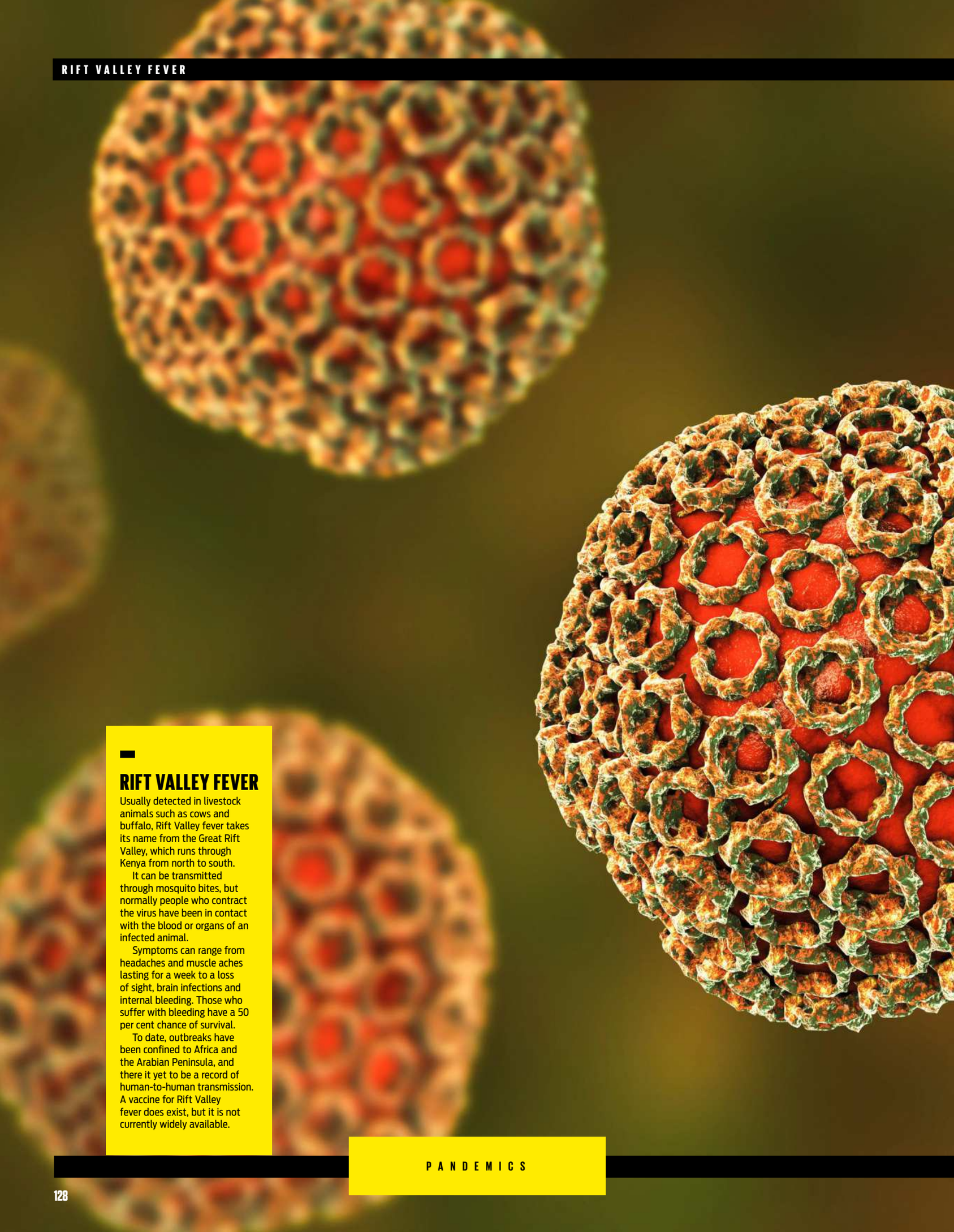
Medicine constitutes a large part of the potential benefits of viruses. Each virus works by invading a host cell, without which it cannot reproduce itself. This is one reason why viruses cannot be considered true forms of life. However, the ability of viral particles (virions) to target specific types of cell opens up tremendous possibilities for cancer treatment (Oncolytic Virus Therapy) and antibacterial tasks.

One of the fantastic characteristics of viruses is their relatively simple anatomy. At their most basic, they are molecules of genetic material surrounded by a protein coat, which makes modifying their genetic structure easier. Their comparatively short DNA means artificially designed genes can be inserted into the native chains, altering the properties and behaviour of the virus. Combined with the fundamental system of virions to inject DNA into cells in a highly selective pattern, they represent a great way of identifying, targeting and destroying cells while leaving neighbouring cells unaffected. By tweaking their genes we can make viruses work for us with extreme precision. This also makes viruses the perfect models for genetic research. A small change to the DNA (or RNA, depending on the strain in question) can be seen quickly reflected in the physical characteristics and behaviour (phenotype).

In circumstances where a patient is suffering from a bacterial infection, modified viruses called bacteriophages can be introduced to destroy the bacterial cells, with no toxicity to body tissues. Some bacteriophages actually exist naturally in the mucus membranes of critical body regions and form part of our standard immune functioning. Without these responses, the times and effectiveness of an immune response would be greatly reduced. Since viruses are able to identify the markers on specific cell types, different strains can be engineered for different infectious bacteria. This has already proven effective, even with body-wide infections, where other conventional antibacterial treatments have been unable to control bacterial populations.

The specificity of virus-targeting mechanisms makes them candidates for pest control too. Since the life-cycle depends on particular insects, introducing virions into crops (as biopesticides) can be guaranteed to reduce pest populations without the issues of groundwater pollution, bioaccumulation or non-target poisoning that are associated with chemical control methods. Insects ingest the particles, which infect their cells selectively. When the insects die they release new viral units, which continue to control the next generation of pests without the need for the reapplication of pesticides.

The viral DNA delivery system is itself of tremendous interest to the scientific community. Normal virus functioning involves the injection of its genetic material into the host cell, which acts as a virus particle factory. The native DNA replication system is hijacked to assemble new viruses. This ability means we can use virions as vectors to carry amended DNA to specific locations. This is highly useful for genetic engineering. The application of viruses in nanotechnology has also shown promise. Particles can be used as 'nanocages' to entrap and store microscopic substances, as well as physical scaffolding. The surface of the protein capsid can be used to support nano structures, which can link together with those on a neighbouring virus to build larger bio-technological architecture.



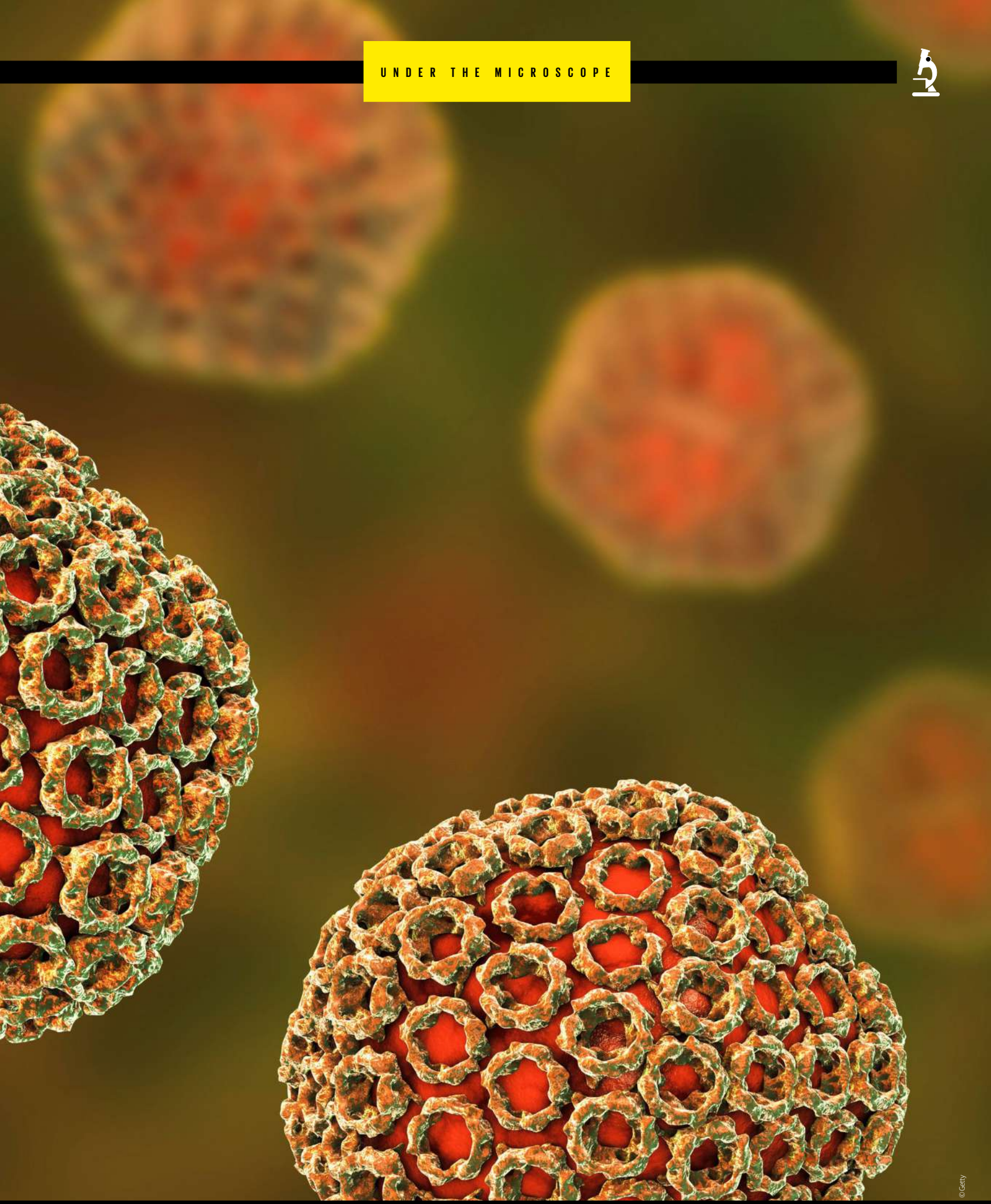
RIFT VALLEY FEVER

Usually detected in livestock animals such as cows and buffalo, Rift Valley fever takes its name from the Great Rift Valley, which runs through Kenya from north to south.

It can be transmitted through mosquito bites, but normally people who contract the virus have been in contact with the blood or organs of an infected animal.

Symptoms can range from headaches and muscle aches lasting for a week to a loss of sight, brain infections and internal bleeding. Those who suffer with bleeding have a 50 per cent chance of survival.

To date, outbreaks have been confined to Africa and the Arabian Peninsula, and there it yet to be a record of human-to-human transmission. A vaccine for Rift Valley fever does exist, but it is not currently widely available.



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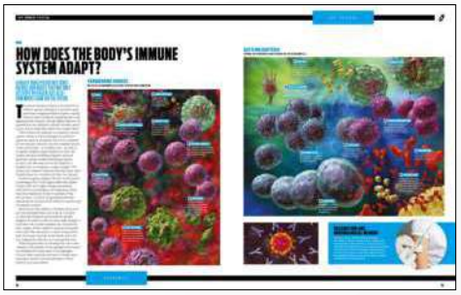
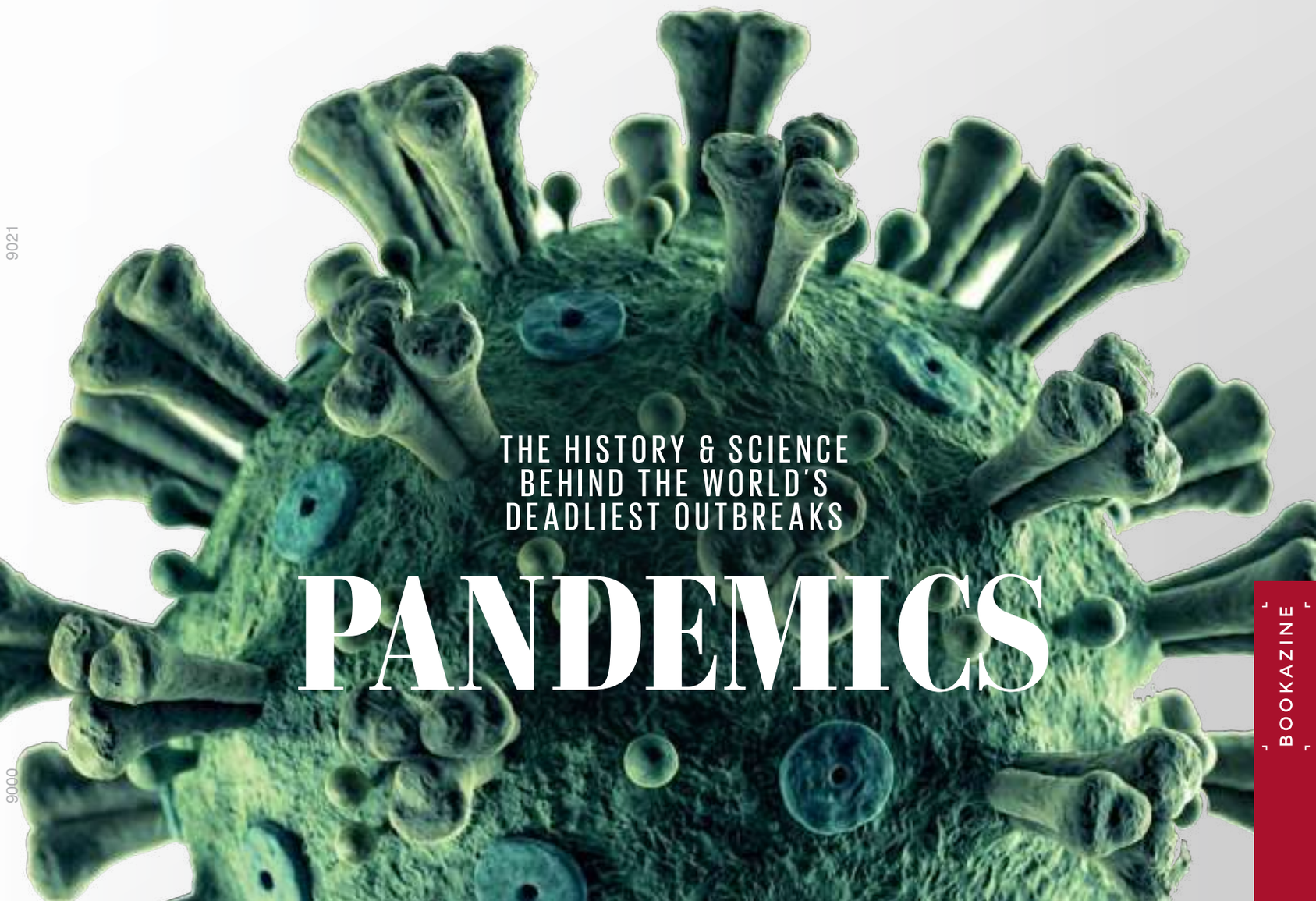


THE IMMUNE SYSTEM

FIND OUT HOW YOUR NATURAL DEFENCES PROTECT YOU FROM DISEASE

COVID-19

UNCOVER THE TRUE IMPACT OF THE VIRUS THAT HAS CHANGED OUR WAY OF LIFE



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